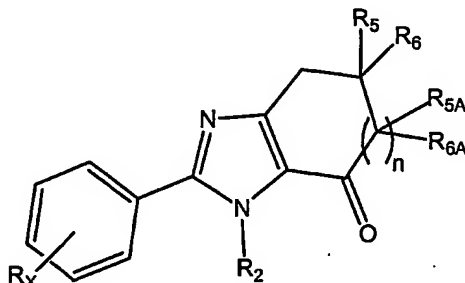


$S(O)_xNH(C_1-C_6 \text{ alkyl})$, $-S(O)_xN(C_1-C_6 \text{ alkyl})(C_1-C_6 \text{ alkyl})$, (where x is 0, 1, or 2).

43. A compound according to Claim 41 of the formula:



wherein:

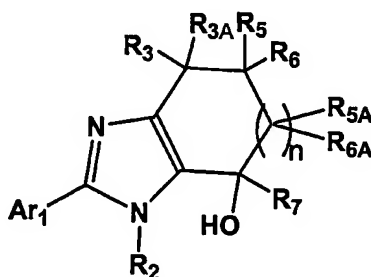
n is 0, 1, or 2:

R_2 is C_3-C_8 straight or branched chain alkyl, C_2-C_8 alkenyl, or C_2-C_8 alkynyl;

R_5 , R_6 , R_{5A} , and R_{6A} are the same or different and represent hydrogen or methyl; and

R_X represents up to four substituents independently chosen from hydrogen, halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1-C_6 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_6 alkoxy, amino, mono- or di(C_1-C_6)alkylamino, and amino(C_1-C_6)alkoxy.

44. A compound of the formula:



wherein:

n is an integer from 0 to 3; and

R_2 is alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl, haloalkyl, each or which may be substituted or unsubstituted;

R_3 and R_{3A} are the same or different and represent hydrogen or alkyl; or

R_3 and R_{3A} , taken together with the carbon atom to which they are attached, form a cycloalkyl ring;

R_5 and R_6 are the same or different and represent hydrogen or alkyl; or

R_5 and R_6 , taken together with the carbon atom to which they are attached, form a cycloalkyl ring;

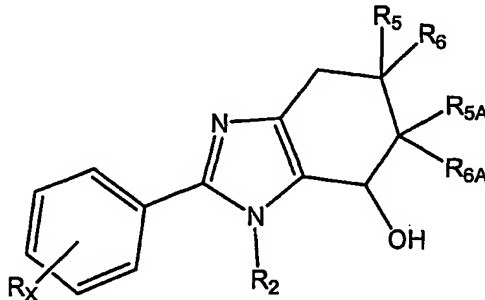
R_{5A} and R_{6A} are the same or different, and are independently selected at each occurrence from hydrogen, halogen, hydroxy, alkyl, and alkoxy;

R_7 represents hydrogen or alkyl; and

Ar_1 is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar_1 is optionally substituted carbocyclic aryl, optionally substituted arylalkyl, or an optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 hetero atoms.

45. A compound according to Claim 44, of the formula:



wherein:

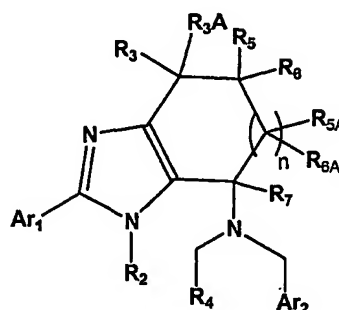
n is an integer from 0 to 3;

R_2 is C_3 - C_8 straight or branched chain alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl;

R_5 , R_6 , R_{5A} , and R_{6A} are the same or different and represent hydrogen or methyl; and

R_X represents up to four substituents independently chosen from hydrogen, halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_2 - C_8 alkenyl, C_2 - C_8 alkynyl, C_1 - C_6 alkoxy, amino, mono- or di(C_1 - C_6)alkylamino, and amino(C_1 - C_6)alkoxy.

46. A process for preparing a compound of the formula:



wherein:

n is an integer from 0 to 3; and

R₂ is hydrogen or

alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl, or haloalkyl, each or which may be substituted or unsubstituted;

R₄ is hydrogen or

alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl, haloalkyl, each or which may be substituted or unsubstituted; or

R₄ is optionally substituted carbocyclic aryl, optionally substituted arylalkyl, or an optionally substituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 hetero atoms,

R₃ and R_{3A} are the same or different and represent hydrogen or alkyl; or

R₃ and R_{3A}, taken together with the carbon atom to which they are attached, form a cycloalkyl ring;

R₅ and R₆ are the same or different and represent hydrogen, halogen, hydroxy, alkyl, or alkoxy; or

R₅ and R₆, taken together with the carbon atom to which they are attached form a cycloalkyl ring;

R_{5A} and R_{6A} are the same or different, and are independently selected at each occurrence from hydrogen, halogen, hydroxy, alkyl, and alkoxy;

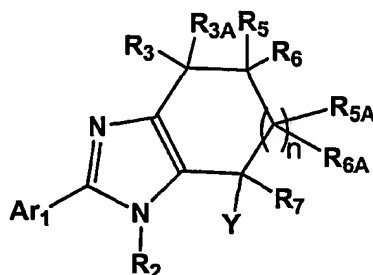
R₇ represents hydrogen or alkyl;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently optionally substituted carbocyclic aryl, optionally substituted arylalkyl, or an optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 hetero atoms.

the process comprising:

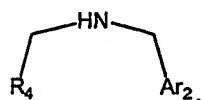
reacting a compound of the formula:



wherein Y is halogen or sulfonate ester,

in a suitable solvent in the presence of a suitable base,

with a secondary amine of the formula:



47. A process according to Claim 46, wherein

n and Y are as defined in Claim 46;

R₃ and R_{3A} are the same or different and represent hydrogen or C₁-C₆ alkyl; or

R₃ and R_{3A}, taken together with the carbon atom to which they are attached, form a C₃₋₈ cycloalkyl ring;

R₅ and R₆ are the same or different and represent hydrogen, halogen, hydroxy, C₁-C₆ alkyl, or C₁-C₆ alkoxy; or

R₅ and R₆, taken together with the carbon atom to which they are attached form a C₃₋₈ cycloalkyl ring;

R_{5a} and R_{6a} are the same or different, and are independently selected at each occurrence from hydrogen, halogen, hydroxy, C₁-C₆ alkyl, and C₁-C₆ alkoxy;

R₂ is hydrogen or

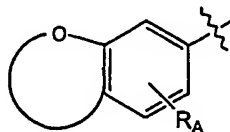
C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈ cycloalkyl, (C₃₋₈ cycloalkyl) C₁₋₃ alkyl, or C₁₋₆ haloalkyl, each or which unsubstituted or substituted by one or more of halogen, nitro, cyano, trifluormethyl, trifluoromethoxy, C₁₋₃ haloalkyl, hydroxy, acetoxy, alkoxy, amino, and mono- or di(C₁₋₆)alkylamino;

R₄ is hydrogen or

C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈cycloalkyl, (C₃₋₈ cycloalkyl)C₁₋₄alkyl, haloalkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, amino and mono- or di(C₁₋₆)alkylamino,

R₄ is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenylalkyl, chromanyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, indanyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinoliny, isoquinoliny, cinnoliny, quinazoliny, or quinoxaliny, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, amino, mono- or di(C₁₋₆)alkylamino, amino(C₁₋₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁₋₆)alkylaminocarbonyl, N-(C₁₋₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl, -X₄R_B, wherein X₄ and R_B are as defined below; or

R₄ is a bicyclic oxygen-containing group of the formula:



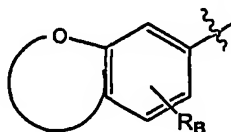
wherein R_A represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_1 - C_6 alkoxy, amino, and mono- or di(C_1 - C_6)alkylamino;

Ar_1 is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar_1 and Ar_2 are independently chosen from

- i) phenyl, phenylalkyl, chromanyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, indanyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinoliny, isoquinoliny, cinnoliny, quinazoliny, or quinoxaliny, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_1 - C_6 alkoxy, amino, mono- or di(C_1 - C_6)alkylamino, amino(C_1 - C_6)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C_1 - C_6)alkylaminocarbonyl, N-(C_1 - C_6)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl, and $-X_4R_B$, wherein X_4 and R_B are as defined below; and

- ii) bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_1 - C_6 alkoxy, amino, and mono- or di(C_1 - C_6)alkylamino;

X_4 is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHRC-$, $-O-$, $-S(O)_m-$, $-NH-$, $-NRC-$, $-C(=O)NH-$, $-C(=O)NRC-$, $-S(O)_mNH-$, $-S(O)_mNRC-$, $-NHC(=O)-$,

$-\text{NR}_\text{C}\text{C}(=\text{O})-$, $-\text{NHS}(\text{O})_\text{m}-$, $-\text{C}(=\text{O})\text{NHS}(\text{O})_\text{m}-$, and $-\text{NR}_\text{C}\text{S}(\text{O})_\text{m}-$ (where m is 0, 1, or 2);

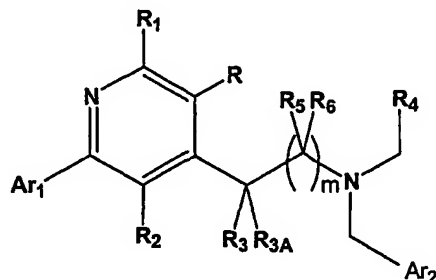
and

R_B and R_C , which may be the same or different, are independently selected at each occurrence from the group consisting of:

hydrogen, straight, branched, or cyclic alkyl groups, which may contain one or more double or triple bonds, each of which may unsubstituted or substituted with one or more substituent(s) selected from:

oxo, hydroxy, $-\text{O}(\text{C}_1\text{-C}_6 \text{ alkyl})$, $-\text{NH}(\text{C}_1\text{-C}_6 \text{ alkyl})$,
 $-\text{N}(\text{C}_1\text{-C}_6 \text{ alkyl})(\text{C}_1\text{-C}_6 \text{ alkyl})$, $-\text{NHC}(\text{O})(\text{C}_1\text{-C}_6 \text{ alkyl})$, $-\text{N}(\text{C}_1\text{-C}_6 \text{ alkyl})\text{C}(\text{O})(\text{C}_1\text{-C}_6 \text{ alkyl})$, $-\text{NHS}(\text{O})_\text{x}(\text{C}_1\text{-C}_6 \text{ alkyl})$, $-\text{S}(\text{O})_\text{x}(\text{C}_1\text{-C}_6 \text{ alkyl})$, $-\text{S}(\text{O})_\text{x}\text{NH}(\text{C}_1\text{-C}_6 \text{ alkyl})$, $-\text{S}(\text{O})_\text{x}\text{N}(\text{C}_1\text{-C}_6 \text{ alkyl})(\text{C}_1\text{-C}_6 \text{ alkyl})$, (where x is 0, 1, or 2).

48. A compound of the formula:



or a pharmaceutically acceptable salt, prodrug or hydrate thereof, wherein:

m is 0, 1, or 2;

R is hydrogen, hydroxy, halogen, amino, cyano, nitro, haloalkyl, alkoxy, mono- or dialkylamino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted (cycloalkyl)alkyl; or

R is optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms;

R₁, R₂, R₃, R_{3A}, R₅, and R₆ are independently selected from hydrogen, hydroxy, halogen, amino, cyano, nitro, haloalkyl, alkoxy, mono- or dialkylamino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, and optionally substituted (cycloalkyl)alkyl;

R₄ is alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl each of which may be optionally substituted; or

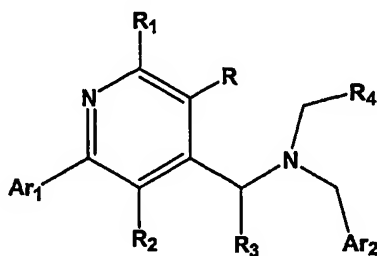
R₄ is optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms; and

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms.

49. A compound according to Claim 48, wherein the compound exhibits an IC₅₀ of 1μM or less in an assay of C5a mediated chemotaxis or calcium mobilization.

50. A compound according to Claim 48 of the formula



wherein Ar₁, Ar₂, R, R₁, R₂, R₃, and R₄ are as defined in Claim 48.

51. A compound according to Claim 50, wherein

R is selected from

i) hydrogen, halogen, hydroxy, amino, alkoxy, mono- or dialkylamino, cyano, nitro, haloalkyl, and

ii) alkyl, alkenyl, alkynyl, cycloalkyl, and (cycloalkyl)alkyl, each of which may be unsubstituted or substituted by one or more of halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkoxy, amino, and mono- or dialkylamino; or

R is selected from

phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino, and mono- or dialkylamino; and

R₁, R₂, and R₃ are independently selected from

i) hydrogen, halogen, hydroxy, amino, alkoxy, mono- or dialkylamino, cyano, nitro, haloalkyl, and
ii) alkyl, alkenyl, alkynyl, cycloalkyl, and (cycloalkyl)alkyl, each of which may be unsubstituted or substituted by one or more of halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkoxy, amino, and mono- or dialkylamino;

R₄ is hydrogen or

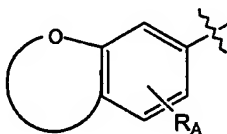
alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl, haloalkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino and mono- or dialkylamino,

R₄ is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenylalkyl, chromanyl,

pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, indanyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl,

cinnolinyl, quinazolinyl, or quinoxalinyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino, mono- or dialkylamino, aminoalkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or dialkylaminocarbonyl, N-alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl, $-X_4R_B$, wherein X_4 and R_B are as defined below; or

R_4 is a bicyclic oxygen-containing group of the formula:



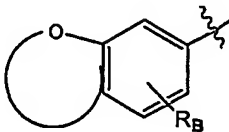
wherein R_A represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino, and mono- or dialkylamino;

Ar_1 is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar_1 and Ar_2 are independently chosen from

- i) phenyl, phenylalkyl, chromanyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, indanyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, or quinoxalinyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino, mono- or dialkylamino, aminoalkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or dialkylaminocarbonyl, N-alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl, and $-X_4R_B$, wherein X_4 and R_B are as defined below; and

ii) bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino, and mono- or dialkylamino;

X_4 is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHR_C-$, $-O-$, $-S(O)_m-$, $-NH-$, $-NR_C-$, $-C(=O)NH-$, $-C(=O)NR_C-$, $-S(O)_mNH-$, $-S(O)_mNR_C-$, $-NHC(=O)-$,

$-NR_C C(=O)-$, $-NHS(O)_m-$, $-C(=O)NHS(O)_m-$, and $-NR_C S(O)_m-$ (where m is 0, 1, or 2);

and

R_B and R_C , which may be the same or different, are independently selected at each occurrence from the group consisting of:

hydrogen, straight, branched, or cyclic alkyl groups, which may contain one or more double or triple bonds, each of which may unsubstituted or substituted with one or more substituent(s) selected from:

oxo, hydroxy, $-O(alkyl)$, $-NH(alkyl)$, $-N(alkyl)(alkyl)$, $-NHC(O)(alkyl)$, $-N(alkyl)C(O)(alkyl)$, $-NHS(O)_x(C_1-C_6 alkyl)$, $-S(O)_x(alkyl)$, $-S(O)_xNH(alkyl)$, $-S(O)_xN(alkyl)(alkyl)$, (where x is 0, 1, or 2).

52. A compound according to Claim 50, wherein

R_1 , R_2 , and R_3 are independently selected from

- i) hydrogen, halogen, hydroxy, amino, C_1-C_6 alkoxy, mono- or di(C_1-C_6)alkylamino, cyano, nitro, haloalkyl, and
- ii) C_1-C_8 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_8 cycloalkyl, and (C_3-C_8 cycloalkyl) C_1-C_3 alkyl, each of which may be unsubstituted or substituted by one or more of halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy,

haloalkyl, hydroxy, acetoxy, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino;

R is selected from

- i) hydrogen, halogen, hydroxy, amino, C₁-C₆ alkoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, haloalkyl, and
- ii) C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, and (C₃-C₈)cycloalkyl) C₁-C₃ alkyl, each of which may be unsubstituted or substituted by one or more of halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkoxy, amino, and mono- or di(C₁-C₆)alkylamino; or

R is selected from

phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino;

R₄ is hydrogen or

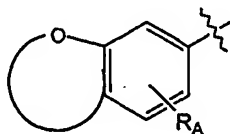
C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈cycloalkyl, (C₃₋₈ cycloalkyl)C₁₋₄alkyl, haloalkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino,

R₄ is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenylalkyl, chromanyl,

pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, indanyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinoliny, isoquinoliny,

cinnolinyl, quinazolinyl, or quinoxalinyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidyl, 1-pyrrolidinyl, 1-piperidyl, -X₄R_B, wherein X₄ and R_B are as defined below; or

R₄ is a bicyclic oxygen-containing group of the formula:



wherein R_A represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino; and

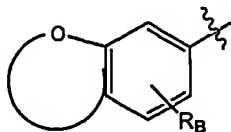
Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently chosen from

- i) phenyl, phenylalkyl, chromanyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, indanyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, or quinoxalinyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(

C₁-C₆alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl, and -X₄R_B, wherein X₄ and R_B are as defined below; and

ii) bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino;

X₄ is independently selected at each occurrence from the group consisting of -CH₂-, -CHRC-, -O-, -S(O)_m-, -NH-, -NR_C-, -C(=O)NH-, -C(=O)NR_C-, -S(O)_mNH-, -S(O)_mNR_C-, -NHC(=O)-, -NR_CC(=O)-, -NHS(O)_m-, -C(=O)NHS(O)_m-, and -NR_CS(O)_m- (where m is 0, 1, or 2); and

R_B and R_C, which may be the same or different, are independently selected at each occurrence from the group consisting of:

hydrogen, straight, branched, or cyclic alkyl groups, which may contain one or more double or triple bonds, each of which may unsubstituted or substituted with one or more substituent(s) selected from:

oxo, hydroxy, -O(C₁-C₆ alkyl), -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)(C₁-C₆ alkyl), -NHC(O)(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)C(O)(C₁-C₆ alkyl), -NHS(O)_x(C₁-C₆ alkyl), -S(O)_x(C₁-C₆ alkyl), -S(O)_xNH(C₁-C₆ alkyl), -S(O)_xN(C₁-C₆ alkyl)(C₁-C₆ alkyl), (where x is 0, 1, or 2).

53. A compound according to Claim 50, wherein:

R is hydrogen, halogen, C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₁-C₈ cycloalkyl, (C₃-C₈cycloalkyl)C₁-C₃alkyl, C₁-C₈ alkoxy, or C₁-C₈ haloalkyl, or

R is a phenyl which may be substituted by up to five substituents independently chosen from C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₁-C₈ alkoxy, halogen, cyano, carboxylic acid, hydroxy, acetoxy, nitro, amino, mono or di(C₁-C₆)alkylamino, aminocarbonyl, sulfonamido, mono or di(C₁-C₆)alkylsulfonamido, 3,4-methylenedioxy, 3,4-(1,2-ethylene)dioxy, trifluoromethyl or trifluoromethoxy;

R₁ is hydrogen, C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₃-C₈ cycloalkyl (C₃-C₈cycloalkyl)C₁-C₃alkyl or C₁-C₈ haloalkyl;

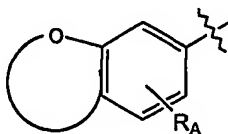
R₂ is C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₁-C₈ cycloalkyl or (C₃-C₈cycloalkyl)C₁-C₃alkyl or C₁-C₈ haloalkyl;

R₃ is hydrogen, C₁-C₈ alkyl, C₂-C₈ alkenyl, or C₂-C₈ alkynyl;

R₄ is C₁-C₈ alkyl, C₃-C₈ cycloalkyl, or (C₃-C₈ cycloalkyl) C₁-C₃ alkyl, each of which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino; or

R₄ is phenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinoliny, isoquinoliny, quinazoliny, or quinoxaliny, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino; or

R₄ is a bicyclic oxygen-containing group of the formula:

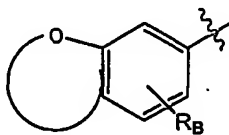


wherein R_A represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino; and

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently chosen from phenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinoliny, isoquinoliny, and quinoxaliny, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidiny, and 1-piperidyl, and

bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino.

54. A compound according to Claim 50, wherein:

R is hydrogen, halogen, C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₁-C₈ cycloalkyl, (C₃-C₈cycloalkyl)C₁-C₃alkyl, C₁-C₈ alkoxy, or C₁-C₈ haloalkyl, or

R is a phenyl which may be substituted by up to five substituents independently chosen from C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₁-C₈ alkoxy, halogen, cyano, carboxylic acid, hydroxy, acetoxy, nitro, amino, mono or di(C₁-C₆)alkylamino, aminocarbonyl, sulfonamido, mono or di(C₁-C₆)alkylsulfonamido, 3,4-methylenedioxy, 3,4-(1,2-ethylene)dioxy, trifluoromethyl or trifluoromethoxy;

R₁ is hydrogen, C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₃-C₈ cycloalkyl (C₃-C₈cycloalkyl)C₁-C₃alkyl or C₁-C₈ haloalkyl;

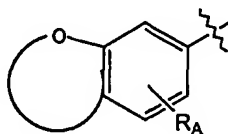
R₂ is C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₁-C₈ cycloalkyl or (C₃-C₈ cycloalkyl)C₁-C₃alkyl or C₁-C₈ haloalkyl;

R₃ is hydrogen, C₁-C₈ alkyl, C₂-C₈ alkenyl, or C₂-C₈ alkynyl;

R₄ is C₁-C₈ alkyl, C₃-C₈ cycloalkyl, or (C₃-C₈ cycloalkyl) C₁-C₃ alkyl, each of which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino; or

R₄ is phenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinoliny, isoquinoliny, quinazoliny, or quinoxaliny, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino; or

R₄ is a bicyclic oxygen-containing group of the formula:

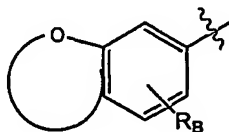


wherein R_A represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, phenyl, thienyl, or pyridyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino; and

Ar₂ is phenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinoliny, isoquinoliny, and quinoxaliny, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidiny, and 1-piperidyl, or

Ar₂ is a bicyclic oxygen-containing group of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino.

55. A compound according to Claim 50, wherein

R is hydrogen, halogen, methyl, ethyl, methoxy, ethoxy, trifluoromethyl, or phenyl;

R₁ is hydrogen, methyl or ethyl;

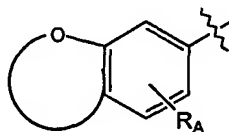
R₂ is C₃-C₆ alkyl;

R₃ is hydrogen, methyl or ethyl;

R₄ is C₁-C₈ alkyl, C₃-C₈ cycloalkyl, or (C₃-C₈ cycloalkyl) C₁-C₃ alkyl, each of which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino; or

R₄ is phenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl, or quinoxalinyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino; or

R₄ is a bicyclic oxygen-containing group of the formula:

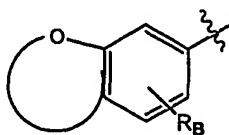


wherein R_A represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, phenyl, thienyl, or pyridyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino; and

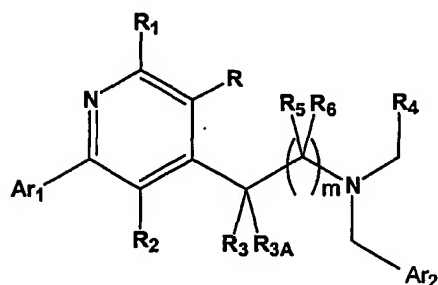
Ar₂ is phenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, and quinoxalinyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino;

Ar₂ is a bicyclic oxygen-containing group of the formula:



wherein R_8 represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_1 - C_6 alkoxy, amino, and mono- or di(C_1 - C_6)alkylamino.

56. A compound of the formula:



wherein:

m is 0, 1, or 2;

R is hydrogen, hydroxy, halogen, amino, cyano, nitro, haloalkyl, alkoxy, mono- or dialkylamino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted (cycloalkyl)alkyl; or

R is optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms;

R_1 , R_2 , R_3 , R_{3A} , R_5 , and R_6 are independently selected from hydrogen, hydroxy, halogen, amino, cyano, nitro, haloalkyl, alkoxy, mono- or dialkylamino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, and optionally substituted (cycloalkyl)alkyl;

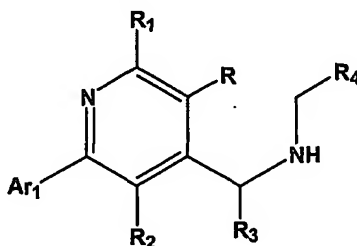
R_4 is alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl each of which may be optionally substituted; or

R_4 is optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms; and

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms.

57. A compound of the formula:



wherein Ar₁, R, R₁, R₂, R₃, R₄ are as defined in Claim 56.

58. A compound according to Claim 56, wherein:

R₁, R₂, and R₃ are independently selected from

- i) hydrogen, halogen, hydroxy, amino, C₁-C₆ alkoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, haloalkyl, and
- ii) C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, and (C₃-C₈ cycloalkyl) C₁-C₃ alkyl, each of which may be unsubstituted or substituted by one or more of halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino;

R is selected from

- i) hydrogen, halogen, hydroxy, amino, C₁-C₆ alkoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, haloalkyl, and
- ii) C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, and (C₃-C₈ cycloalkyl) C₁-C₃ alkyl, each of which may be unsubstituted or substituted by one or more of halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkoxy, amino, and mono- or di(C₁-C₆)alkylamino; or

R is selected from

phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino;

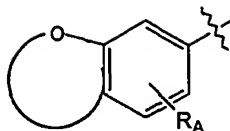
R₄ is hydrogen or

C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈cycloalkyl, (C₃₋₈ cycloalkyl)C₁₋₄alkyl, haloalkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino,

R₄ is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenylalkyl, chromanyl,

pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, indanyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, or quinoxaliny, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl, -X₄R_B, wherein X₄ and R_B are as defined below; or

R₄ is a bicyclic oxygen-containing group of the formula:



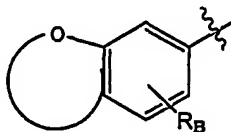
wherein R_A represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_1 - C_6 alkoxy, amino, and mono- or di(C_1 - C_6)alkylamino; and

Ar_1 is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar_1 and Ar_2 are independently chosen from

- i) phenyl, phenylalkyl, chromanyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, indanyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinoliny, isoquinoliny, cinnoliny, quinazoliny, or quinoxaliny, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_1 - C_6 alkoxy, amino, mono- or di(C_1 - C_6)alkylamino, amino(C_1 - C_6)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C_1 - C_6)alkylaminocarbonyl, N-(C_1 - C_6)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl, and $-X_4R_B$, wherein X_4 and R_B are as defined below; and

- ii) bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_1 - C_6 alkoxy, amino, and mono- or di(C_1 - C_6)alkylamino;

X_4 is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHRC-$, $-O-$, $-S(O)_m-$, $-NH-$, $-NRC-$, $-C(=O)NH-$, $-C(=O)NRC-$, $-S(O)_mNH-$, $-S(O)_mNRC-$, $-NHC(=O)-$, $-NRC(=O)-$, $-NHS(O)_m-$, $-C(=O)NHS(O)_m-$, and $-NRC(=O)S(O)_m-$ (where m is 0, 1, or 2); and

R_B and R_C , which may be the same or different, are independently selected at each occurrence from the group consisting of:

hydrogen, straight, branched, or cyclic alkyl groups, which may contain one or more double or triple bonds, each of which may unsubstituted or substituted with one or more substituent(s) selected from:

oxo, hydroxy, $-O(C_1-C_6 \text{ alkyl})$, $-NH(C_1-C_6 \text{ alkyl})$, $-N(C_1-C_6 \text{ alkyl})(C_1-C_6 \text{ alkyl})$, $-NHC(O)(C_1-C_6 \text{ alkyl})$, $-N(C_1-C_6 \text{ alkyl})C(O)(C_1-C_6 \text{ alkyl})$, $-NHS(O)_x(C_1-C_6 \text{ alkyl})$, $-S(O)_x(C_1-C_6 \text{ alkyl})$, $-S(O)_xNH(C_1-C_6 \text{ alkyl})$, $-S(O)_xN(C_1-C_6 \text{ alkyl})(C_1-C_6 \text{ alkyl})$, (where x is 0, 1, or 2).

59. A compound according to Claim 56, wherein:

R is hydrogen, halogen, methyl, ethyl, methoxy, ethoxy, trifluoromethyl, or phenyl;

R_1 is hydrogen, methyl or ethyl;

R_2 is C_3-C_6 alkyl;

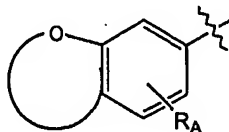
R_3 is hydrogen, methyl or ethyl;

R_4 is C_1-C_8 alkyl, C_3-C_8 cycloalkyl, or $(C_3-C_8 \text{ cycloalkyl}) C_1-C_3$ alkyl, each of which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy, amino, and mono- or di(C_1-C_6)alkylamino; or

R_4 is phenyl, phenyl(C_1-C_4)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl, or quinoxalinyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl,

trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino; or

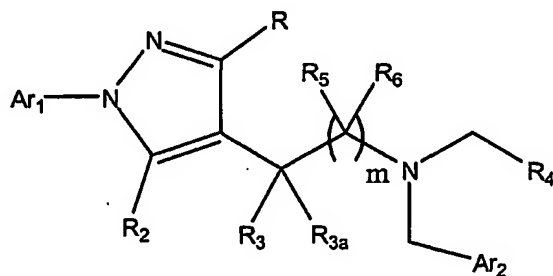
R₄ is a bicyclic oxygen-containing group of the formula:



wherein R_A represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino; and

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, phenyl, thienyl, or pyridyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino.

60. A compound of the formula:



or pharmaceutically acceptable salt, prodrug or hydrate thereof, wherein:

m is 0, 1, or 2;

R is chosen from hydrogen, hydroxy, halogen, amino, cyano, nitro, haloalkyl, alkoxy, mono- or dialkylamino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted (cycloalkyl)alkyl,

optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms;

R₂, R₃, R_{3A}, R₅, and R₆ are independently selected from hydrogen, hydroxy, halogen, amino, cyano, nitro, haloalkyl, alkoxy, mono- or dialkylamino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, and optionally substituted (cycloalkyl)alkyl;

R and R₃ may be joined to form an optionally substituted saturated carbocyclic ring of from 5 to 8 members or an optionally substituted heterocyclic ring of from 5 to 8 members;

R₄ is alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl each of which may be optionally substituted; or

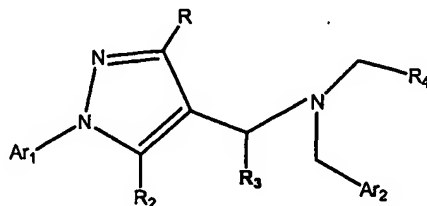
R₄ is optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms; and

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms.

61. A compound according to Claim 60, wherein the compound exhibits an IC₅₀ of 1μM or less in an assay of C5a mediated chemotaxis or calcium mobilization.

62. A compound according of the formula:



or a pharmaceutically acceptable salt, prodrug or hydrate thereof, wherein:

R is chosen from hydrogen, hydroxy, halogen, amino, cyano, nitro, haloalkyl, alkoxy, mono- or dialkylamino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted (cycloalkyl)alkyl, optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms;

R₂ and R₃ are independently selected from hydrogen, hydroxy, halogen, amino, cyano, nitro, haloalkyl, alkoxy, mono- or dialkylamino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, and optionally substituted (cycloalkyl)alkyl;

R and R₃ may be joined to form an optionally substituted carbocyclic ring of from 5 to 8 members or an optionally substituted heterocyclic ring of from 5 to 8 members;

R₄ is alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl each of which may be optionally substituted; or

R₄ is optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms; and

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms.

63. A compound according to Claim 62, wherein R and R₃ are not joined.

64. A compound according to Claim 62, wherein:

R is selected from

- i) hydrogen, halogen, hydroxy, amino, alkoxy, mono- or dialkylamino, cyano, nitro, haloalkyl, and
- ii) alkyl, alkenyl, alkynyl, cycloalkyl, and (cycloalkyl)alkyl, each of which may be unsubstituted or substituted by one or more of halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkoxy, amino, and mono- or dialkylamino,
- iii) phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, each of which may be substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino, and mono- or dialkylamino;

R₂ and R₃ are independently selected from

- i) hydrogen, halogen, hydroxy, amino, alkoxy, mono- or dialkylamino, cyano, nitro, haloalkyl, and
- ii) alkyl, alkenyl, alkynyl, cycloalkyl, and (cycloalkyl)alkyl, each of which may be unsubstituted or substituted by one or more of halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkoxy, amino, and mono- or dialkylamino;

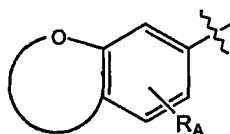
R₄ is hydrogen or

alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl, haloalkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino and mono- or dialkylamino,

R₄ is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenylalkyl, chromanyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, indanyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benzodioxanyl,

benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, or quinoxalinyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino, mono- or dialkylamino, aminoalkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or dialkylaminocarbonyl, N-alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl and -X₄R_B, wherein X₄ and R_B are as defined below; or

R₄ is a bicyclic oxygen-containing group of the formula:



wherein R_A represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino, and mono- or dialkylamino;

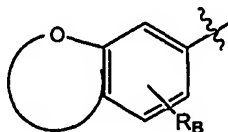
Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently chosen from

- i) phenyl, phenylalkyl, chromanyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, indanyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, or quinoxalinyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino, mono- or dialkylamino, aminoalkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or dialkylaminocarbonyl, N-

alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl and –
 X_4R_B , wherein X_4 and R_B are as defined below; and

ii) bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino, and mono- or dialkylamino;

X_4 is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHRC-$, $-O-$, $-S(O)_m-$, $-NH-$, $-NRC-$, $-C(=O)NH-$, $-C(=O)NRC-$, $-S(O)_mNH-$, $-S(O)_mNRC-$, $-NHC(=O)-$, $-NRC(=O)-$, $-NHS(O)_m-$, $-C(=O)NHS(O)_m-$, and $-NRC(=O)S(O)_m-$ (where m is 0, 1, or 2); and

R_B and R_C , which may be the same or different, are independently selected at each occurrence from the group consisting of:

hydrogen, straight, branched, or cyclic alkyl groups, which may contain one or more double or triple bonds, each of which may unsubstituted or substituted with one or more substituent(s) selected from:

oxo, hydroxy, $-O(alkyl)$, $-NH(alkyl)$, $-N(alkyl)(alkyl)$, $-NHC(O)(alkyl)$, $-N(alkyl)C(O)(alkyl)$, $-NHS(O)_x(alkyl)$, $-S(O)_x(alkyl)$, $-S(O)_xNH(alkyl)$, $-S(O)_xN(alkyl)(alkyl)$, (where x is 0, 1, or 2).

65. A compound according to Claim 62, wherein:

R is selected from

- i) hydrogen, halogen, hydroxy, amino, C_1 - C_6 alkoxy, mono- or di(C_1 - C_6)alkylamino, cyano, nitro, haloalkyl, and
- ii) C_1 - C_8 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_8 cycloalkyl, and (C_3 - C_8)cycloalkyl) C_1 - C_3 alkyl, each of which may be unsubstituted or substituted by one or more of halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy,

haloalkyl, hydroxy, acetoxy, alkoxy, amino, and mono- or di(C₁-C₆)alkylamino,

iii) phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino;

R₂ and R₃ are independently selected from

i) hydrogen, halogen, hydroxy, amino, C₁-C₆ alkoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, haloalkyl, and

ii) C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, and (C₃-C₈ cycloalkyl) C₁-C₃ alkyl, each of which may be unsubstituted or substituted by one or more of halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino;

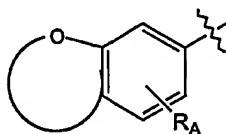
R₄ is hydrogen or

C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈cycloalkyl, (C₃₋₈ cycloalkyl)C₁₋₄alkyl, haloalkyl, each of which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino,

R₄ is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenylalkyl, chromanyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, indanyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinoliny, isoquinoliny, cinnoliny, quinazoliny, or quinoxaliny, each of which may be optionally

substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidiny, 1-piperidyl, -X₄R_B, wherein X₄ and R_B are as defined below; or

R₄ is a bicyclic oxygen-containing group of the formula:



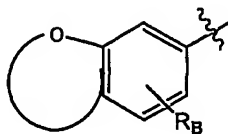
wherein R_A represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently chosen from

- i) phenyl, phenylalkyl, chromanyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, indanyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinoliny, isoquinoliny, cinnoliny, quinazoliny, or quinoxaliny, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidiny, 1-piperidyl, and -X₄R_B, wherein X₄ and R_B are as defined below; and

ii) bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_1 - C_6 alkoxy, amino, and mono- or di(C_1 - C_6)alkylamino;

X_4 is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CH(R_C)-$, $-O-$, $-S(O)_m-$, $-NH-$, $-NR_C-$, $-C(=O)NH-$, $-C(=O)NR_C-$, $-S(O)_mNH-$, $-S(O)_mNR_C-$, $-NHC(=O)-$, $-NR_CC(=O)-$, $-NHS(O)_m-$, $-C(=O)NHS(O)_m-$, and $-NR_CS(O)_m-$ (where m is 0, 1, or 2); and

R_B and R_C , which may be the same or different, are independently selected at each occurrence from the group consisting of:

hydrogen, straight, branched, or cyclic alkyl groups, which may contain one or more double or triple bonds, each of which may unsubstituted or substituted with one or more substituent(s) selected from:

oxo, hydroxy, $-O(C_1-C_6 \text{ alkyl})$, $-NH(C_1-C_6 \text{ alkyl})$, $-N(C_1-C_6 \text{ alkyl})(C_1-C_6 \text{ alkyl})$, $-NHC(O)(C_1-C_6 \text{ alkyl})$, $-N(C_1-C_6 \text{ alkyl})C(O)(C_1-C_6 \text{ alkyl})$, $-NHS(O)_x(C_1-C_6 \text{ alkyl})$, $-S(O)_x(C_1-C_6 \text{ alkyl})$, $-S(O)_xNH(C_1-C_6 \text{ alkyl})$, $-S(O)_xN(C_1-C_6 \text{ alkyl})(C_1-C_6 \text{ alkyl})$, (where x is 0, 1, or 2).

66. A compound according to Claim 62, wherein:

R is hydrogen, halogen, hydroxy, C_1 - C_6 alkoxy, haloalkyl, C_1 - C_8 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_8 cycloalkyl, and (C_3-C_8) cycloalkyl C_1 - C_3 alkyl, or

R is phenyl substituted with up to five groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_8 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_1 - C_6 alkoxy, amino, and mono- or

di(C₁-C₆)alkylamino, aminocarbonyl, sulfonamido, mono or di(C₁-C₆)alkylsulfonamido, 3,4-methylenedioxy, and 3,4-(1,2-ethylene)dioxy;

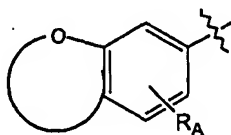
R₂ is selected from C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, (C₃-C₈ cycloalkyl) C₁-C₃ alkyl and haloalkyl;

R₃ is hydrogen C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl;

R₄ is C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈cycloalkyl, (C₃₋₈ cycloalkyl)C₁₋₄alkyl, haloalkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino,

R₄ is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, each of which may be substituted with up to five groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidyl, 1-pyrrolidinyl, 1-piperidyl,

R₄ is a bicyclic oxygen-containing group of the formula:



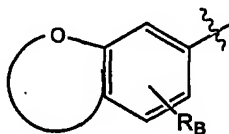
wherein R_A represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently chosen from

- i) phenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, and benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl; or

- ii) bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino.

67. A compound according to Claim 66, wherein

R, R₂, R₃, R₄, and Ar₂ are as defined in Claim 66;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or phenyl with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, and amino(C₁-C₆)alkoxy.

68. A compound according to Claim 66, wherein:

R, R₂, and R₃ are as defined in Claim 66;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or phenyl with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl,

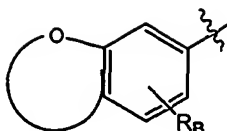
trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, and amino(C₁-C₆)alkoxy;

R₄ is C₃-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₃-C₈cycloalkyl, (C₃₋₈ cycloalkyl)C₁-C₄alkyl, C₁-C₈ haloalkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino,

R₄ is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl;

Ar₂ is phenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, or benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl; or

Ar₂ is bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_1 - C_6 alkoxy, amino, and mono- or di(C_1 - C_6)alkylamino.

69. A compound according to Claim 66, wherein:

R is hydrogen, C_1 - C_8 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_8 cycloalkyl, or (C_3 - C_8)cycloalkyl) C_1 - C_3 alkyl, or

R is phenyl substituted with up to five groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_8 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_1 - C_6 alkoxy, amino, and mono- or di(C_1 - C_6)alkylamino, aminocarbonyl, sulfonamido, mono or di(C_1 - C_6)alkylsulfonamido, 3,4-methylenedioxy, and 3,4-(1,2-ethylene)dioxy;

R_2 is C_3 - C_6 alkyl;

R_3 is hydrogen, methyl, or ethyl;

R_4 is C_3 - C_8 alkyl, C_2 - C_8 alkenyl, C_2 - C_8 alkynyl, C_3 - C_8 cycloalkyl, (C_3 - C_8 cycloalkyl) C_1 - C_4 alkyl, C_1 - C_8 haloalkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_1 - C_6 alkoxy, amino and mono- or di(C_1 - C_6)alkylamino,

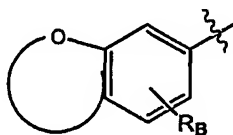
R_4 is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenyl(C_1 - C_4)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_1 - C_6 alkoxy, amino, mono- or di(C_1 -

C₆alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidiny, 1-piperidyl;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or phenyl with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, and amino(C₁-C₆)alkoxy;

Ar₂ is phenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, or benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidiny, 1-piperidyl; or

Ar₂ is bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino.

70. A compound according to Claim 66, wherein:

R is hydrogen, C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, or (C₃-C₈)cycloalkyl) C₁-C₃ alkyl, or phenyl;

R₂ is C₃-C₆ alkyl;

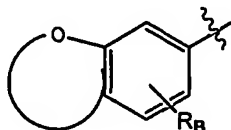
R₃ is hydrogen, methyl, or ethyl;

R₄ is C₃-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₃-C₈cycloalkyl, (C₃₋₈ cycloalkyl)C₁-C₄alkyl, C₁-C₈ haloalkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or phenyl with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, and amino(C₁-C₆)alkoxy; and

Ar₂ is phenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, or benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl; or

Ar₂ is bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino.

71. A compound according to Claim 66, wherein:

R is hydrogen, C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, or (C₃-C₈)cycloalkyl) C₁-C₃ alkyl, or phenyl;

R₂ is C₃-C₆ alkyl;

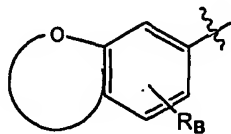
R₃ is hydrogen, methyl, or ethyl;

R₄ is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or phenyl with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, and amino(C₁-C₆)alkoxy;

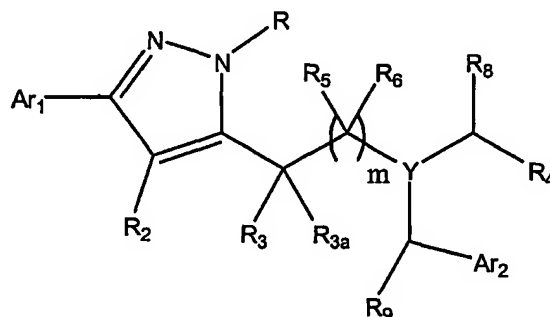
Ar₂ is phenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, or benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl; or

Ar₂ is bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino.

72. A compound of the formula:



or pharmaceutically acceptable salt, prodrug or hydrate thereof, wherein:

m is 0, 1, or 2;

R is chosen from hydrogen, hydroxy, halogen, amino, cyano, nitro, haloalkyl, alkoxy, mono- or dialkylamino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted (cycloalkyl)alkyl, optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms;

R₂, R₃, R_{3A}, R₅, and R₆ are independently selected from hydrogen, hydroxy, halogen, amino, cyano, nitro, haloalkyl, alkoxy, mono- or dialkylamino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, and optionally substituted (cycloalkyl)alkyl;

R and R₃ may be joined to form an optionally substituted saturated carbocyclic ring of from 5 to 8 members or an optionally substituted heterocyclic ring of from 5 to 8 members;

R₄ is alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl each of which may be optionally substituted; or

R₄ is optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms; and

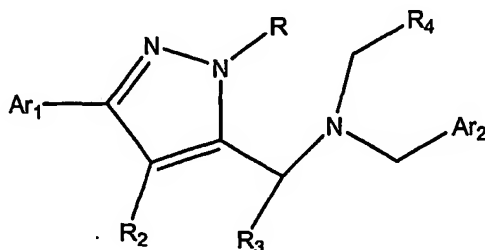
R₈ and R₉ are independently chosen from H or optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, (cycloalkyl)alkyl, haloalkyl, or the like.

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms.

73. A compound according to Claim 72, wherein the compound exhibits an IC₅₀ of 1μM or less in an assay of C5a mediated chemotaxis or calcium mobilization.

74. A compound according of the formula:



or a pharmaceutically acceptable salt, prodrug or hydrate thereof, wherein:

R is chosen from hydrogen, hydroxy, halogen, amino, cyano, nitro, haloalkyl, alkoxy, mono- or dialkylamino, optionally substituted alkyl, optionally substituted

alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted (cycloalkyl)alkyl, optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms;

R₂ and R₃ are independently selected from hydrogen, hydroxy, halogen, amino, cyano, nitro, haloalkyl, alkoxy, mono- or dialkylamino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, and optionally substituted (cycloalkyl)alkyl;

R and R₃ may be joined to form an optionally substituted carbocyclic ring of from 5 to 8 members or an optionally substituted heterocyclic ring of from 5 to 8 members;

R₄ is alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl each of which may be optionally substituted; or

R₄ is optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms; and

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms.

75. A compound according to Claim 74, wherein R and R₃ are not joined.

76. A compound according to Claim 74, wherein:

R is selected from

i) hydrogen, halogen, hydroxy, amino, alkoxy, mono- or dialkylamino, cyano, nitro, haloalkyl, and

ii) alkyl, alkenyl, alkynyl, cycloalkyl, and (cycloalkyl)alkyl, each of which may be unsubstituted or substituted by one or more of halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkoxy, amino, and mono- or dialkylamino,

iii) phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, each of which may be substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino, and mono- or dialkylamino;

R₂ and R₃ are independently selected from

i) hydrogen, halogen, hydroxy, amino, alkoxy, mono- or dialkylamino, cyano, nitro, haloalkyl, and

ii) alkyl, alkenyl, alkynyl, cycloalkyl, and (cycloalkyl)alkyl, each of which may be unsubstituted or substituted by one or more of halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkoxy, amino, and mono- or dialkylamino;

R₄ is hydrogen or

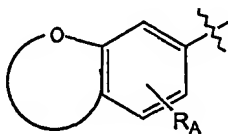
alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl, haloalkyl, each of which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino and mono- or dialkylamino,

R₄ is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenylalkyl, chromanyl,

pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, indanyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinoliny, isoquinoliny, cinnoliny, quinazoliny, or quinoxaliny, each of which may be optionally

substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino, mono- or dialkylamino, aminoalkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or dialkylaminocarbonyl, N-alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidiny, 1-piperidyl and – X_4R_B , wherein X_4 and R_B are as defined below; or

R_4 is a bicyclic oxygen-containing group of the formula:



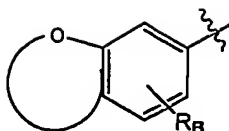
wherein R_A represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino, and mono- or dialkylamino;

Ar_1 is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar_1 and Ar_2 are independently chosen from

- i) phenyl, phenylalkyl, chromanyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, indanyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinoliny, isoquinoliny, cinnoliny, quinazoliny, or quinoxaliny, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino, mono- or dialkylamino, aminoalkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or dialkylaminocarbonyl, N-alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidiny, 1-piperidyl and – X_4R_B , wherein X_4 and R_B are as defined below; and

- ii) bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino, and mono- or dialkylamino;

X_4 is independently selected at each occurrence from the group consisting of $-\text{CH}_2-$, $-\text{CHRC}-$, $-\text{O}-$, $-\text{S(O)}_m-$, $-\text{NH}-$, $-\text{NRC}-$, $-\text{C(=O)NH}-$, $-\text{C(=O)NRC}-$, $-\text{S(O)}_m\text{NH}-$, $-\text{S(O)}_m\text{NRC}-$, $-\text{NHC(=O)}-$, $-\text{NRC(=O)}-$, $-\text{NHS(O)}_m-$, $-\text{C(=O)NHS(O)}_m-$, and $-\text{NRC(=O)S(O)}_m-$ (where m is 0, 1, or 2); and

R_B and R_C , which may be the same or different, are independently selected at each occurrence from the group consisting of:

hydrogen, straight, branched, or cyclic alkyl groups, which may contain one or more double or triple bonds, each of which may unsubstituted or substituted with one or more substituent(s) selected from:

oxo, hydroxy, $-\text{O(alkyl)}$, $-\text{NH(alkyl)}$, $-\text{N(alkyl)(alkyl)}$, $-\text{NHC(O)(alkyl)}$, $-\text{N(alkyl)C(O)(alkyl)}$, $-\text{NHS(O)}_x\text{(alkyl)}$, $-\text{S(O)}_x\text{(alkyl)}$, $-\text{S(O)}_x\text{NH(alkyl)}$, $-\text{S(O)}_x\text{N(alkyl)(alkyl)}$, (where x is 0, 1, or 2).

77. A compound according to Claim 74, wherein:

R is selected from

- i) hydrogen, halogen, hydroxy, amino, C_1 - C_6 alkoxy, mono- or di(C_1 - C_6)alkylamino, cyano, nitro, haloalkyl, and
- ii) C_1 - C_8 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_8 cycloalkyl, and (C_3 - C_8)cycloalkyl) C_1 - C_3 alkyl, each of which may be unsubstituted or substituted by one or more of halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkoxy, amino, and mono- or di(C_1 - C_6)alkylamino,

iii) phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino;

R₂ and R₃ are independently selected from

i) hydrogen, halogen, hydroxy, amino, C₁-C₆ alkoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, haloalkyl, and

ii) C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, and (C₃-C₈ cycloalkyl) C₁-C₃ alkyl, each of which may be unsubstituted or substituted by one or more of halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino;

R₄ is hydrogen or

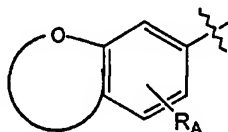
C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈cycloalkyl, (C₃₋₈ cycloalkyl)C₁₋₄alkyl, haloalkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino,

R₄ is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenylalkyl, chromanyl,

pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, indanyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinoliny, isoquinoliny, cinnoliny, quinazoliny, or quinoxaliny, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl,

hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidiny, 1-piperidyl, -X₄R_B, wherein X₄ and R_B are as defined below; or

R₄ is a bicyclic oxygen-containing group of the formula:



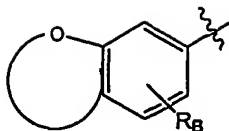
wherein R_A represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently chosen from

- i) phenyl, phenylalkyl, chromanyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, indanyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinoliny, isoquinoliny, cinnoliny, quinazoliny, or quinoxaliny, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidiny, 1-piperidyl, and -X₄R_B, wherein X₄ and R_B are as defined below; and

- ii) bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_1 - C_6 alkoxy, amino, and mono- or di(C_1 - C_6)alkylamino;

X_4 is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHRC-$, $-O-$, $-S(O)_m-$, $-NH-$, $-NRC-$, $-C(=O)NH-$, $-C(=O)NRC-$, $-S(O)_mNH-$, $-S(O)_mNRC-$, $-NHC(=O)-$, $-NRC-C(=O)-$, $-NHS(O)_m-$, $-C(=O)NHS(O)_m-$, and $-NRC-S(O)_m-$ (where m is 0, 1, or 2); and

R_B and R_C , which may be the same or different, are independently selected at each occurrence from the group consisting of:

hydrogen, straight, branched, or cyclic alkyl groups, which may contain one or more double or triple bonds, each of which may unsubstituted or substituted with one or more substituent(s) selected from:

oxo, hydroxy, $-O(C_1-C_6 \text{ alkyl})$, $-NH(C_1-C_6 \text{ alkyl})$, $-N(C_1-C_6 \text{ alkyl})(C_1-C_6 \text{ alkyl})$, $-NHC(O)(C_1-C_6 \text{ alkyl})$, $-N(C_1-C_6 \text{ alkyl})C(O)(C_1-C_6 \text{ alkyl})$, $-NHS(O)_x(C_1-C_6 \text{ alkyl})$, $-S(O)_x(C_1-C_6 \text{ alkyl})$, $-S(O)_xNH(C_1-C_6 \text{ alkyl})$, $-S(O)_xN(C_1-C_6 \text{ alkyl})(C_1-C_6 \text{ alkyl})$, (where x is 0, 1, or 2).

78. A compound according to Claim 74, wherein:

R is hydrogen, halogen, hydroxy, C_1 - C_6 alkoxy, haloalkyl, C_1 - C_8 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_8 cycloalkyl, and (C_3-C_8) cycloalkyl C_1 - C_3 alkyl, or

R is phenyl substituted with up to five groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_8 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_1 - C_6 alkoxy, amino, and mono- or

di(C₁-C₆)alkylamino, aminocarbonyl, sulfonamido, mono or di(C₁-

C₆)alkylsulfonamido, 3,4-methylenedioxy, and 3,4-(1,2-ethylene)dioxy;

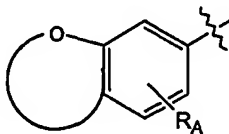
R₂ is selected from C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, (C₃-C₈ cycloalkyl) C₁-C₃ alkyl and haloalkyl;

R₃ is hydrogen C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl;

R₄ is C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈cycloalkyl, (C₃₋₈ cycloalkyl)C₁₋₄alkyl, haloalkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino,

R₄ is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, each of which may be substituted with up to five groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl,

R₄ is a bicyclic oxygen-containing group of the formula:

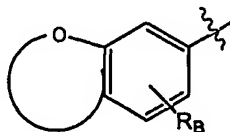


wherein R_A represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently chosen from

- i) phenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, and benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl; or
- ii) bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino.

79. A compound according to Claim 78, wherein

R, R₂, R₃, R₄, and Ar₂ are as defined in Claim 78;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or phenyl with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, and amino(C₁-C₆)alkoxy.

80. A compound according to Claim 78, wherein:

R, R₂, and R₃ are as defined in Claim 78;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or phenyl with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl,

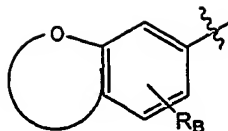
trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, and amino(C₁-C₆)alkoxy;

R₄ is C₃-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₃-C₈cycloalkyl, (C₃₋₈ cycloalkyl)C₁-C₄alkyl, C₁-C₈ haloalkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino,

R₄ is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl;

Ar₂ is phenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, or benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl; or

Ar₂ is bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_1 - C_6 alkoxy, amino, and mono- or di(C_1 - C_6)alkylamino.

81. A compound according to Claim 78, wherein:

R is hydrogen, C_1 - C_8 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_8 cycloalkyl, or (C_3 - C_8)cycloalkyl) C_1 - C_3 alkyl, or

R is phenyl substituted with up to five groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_8 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_1 - C_6 alkoxy, amino, and mono- or di(C_1 - C_6)alkylamino, aminocarbonyl, sulfonamido, mono or di(C_1 - C_6)alkylsulfonamido, 3,4-methylenedioxy, and 3,4-(1,2-ethylene)dioxy;

R_2 is C_3 - C_6 alkyl;

R_3 is hydrogen, methyl, or ethyl;

R_4 is C_3 - C_8 alkyl, C_2 - C_8 alkenyl, C_2 - C_8 alkynyl, C_3 - C_8 cycloalkyl, (C_3 - C_8 cycloalkyl) C_1 - C_4 alkyl, C_1 - C_8 haloalkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_1 - C_6 alkoxy, amino and mono- or di(C_1 - C_6)alkylamino,

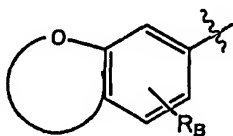
R_4 is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenyl(C_1 - C_4)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_1 - C_6 alkoxy, amino, mono- or di(C_1 -

C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or phenyl with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, and amino(C₁-C₆)alkoxy;

Ar₂ is phenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, or benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl; or

Ar₂ is bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino.

82. A compound according to Claim 78, wherein:

R is hydrogen, C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, or (C₃-C₈)cycloalkyl) C₁-C₃ alkyl, or phenyl;

R₂ is C₃-C₆ alkyl;

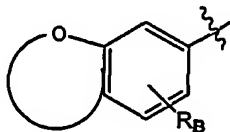
R₃ is hydrogen, methyl, or ethyl;

R₄ is C₃-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₃-C₈cycloalkyl, (C₃₋₈ cycloalkyl)C₁-C₄alkyl, C₁-C₈ haloalkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or phenyl with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, and amino(C₁-C₆)alkoxy; and

Ar₂ is phenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, or benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl; or

Ar₂ is bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino.

83. A compound according to Claim 78, wherein:

R is hydrogen, C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, or (C₃-C₈)cycloalkyl) C₁-C₃ alkyl, or phenyl;

R₂ is C₃-C₆ alkyl;

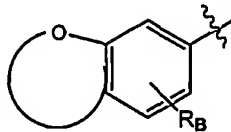
R₃ is hydrogen, methyl, or ethyl;

R₄ is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or phenyl with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, and amino(C₁-C₆)alkoxy;

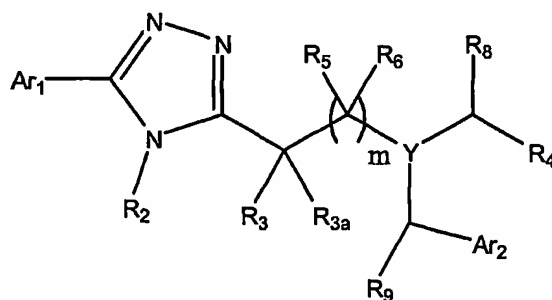
Ar₂ is phenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, or benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl; or

Ar₂ is bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino.

84. A compound of the formula:



or pharmaceutically acceptable salt, prodrug or hydrate thereof, wherein:

m is 0, 1, or 2;

R₂, R₃, R_{3a}, R₅, and R₆ are independently selected from hydrogen, hydroxy, halogen, amino, cyano, nitro, haloalkyl, alkoxy, mono- or dialkylamino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, and optionally substituted (cycloalkyl)alkyl;

R₄ is alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl each of which may be optionally substituted; or

R₄ is optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms; and

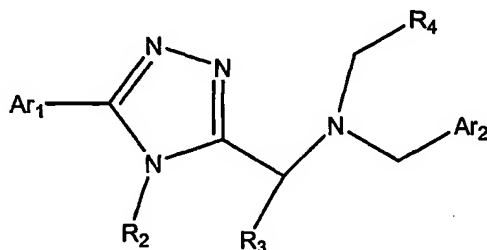
R₈ and R₉ are independently chosen from H or optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, (cycloalkyl)alkyl, haloalkyl, or the like.

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms.

85. A compound according to Claim 84, wherein the compound exhibits an IC₅₀ of 1μM or less in an assay of C5a mediated chemotaxis or calcium mobilization.

86. A compound according of the formula:



or a pharmaceutically acceptable salt, prodrug or hydrate thereof, wherein:

R₂ and R₃ are independently selected from hydrogen, hydroxy, halogen, amino, cyano, nitro, haloalkyl, alkoxy, mono- or dialkylamino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, and optionally substituted (cycloalkyl)alkyl;

R₄ is alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl each of which may be optionally substituted; or

R₄ is optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms; and

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms.

87. A compound according to Claim 86, wherein:

R is selected from

- i) hydrogen, halogen, hydroxy, amino, alkoxy, mono- or dialkylamino, cyano, nitro, haloalkyl, and
- ii) alkyl, alkenyl, alkynyl, cycloalkyl, and (cycloalkyl)alkyl, each of which may be unsubstituted or substituted by one or more of halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkoxy, amino, and mono- or dialkylamino,
- iii) phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, each of which may be substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino, and mono- or dialkylamino;

R₂ and R₃ are independently selected from

- i) hydrogen, halogen, hydroxy, amino, alkoxy, mono- or dialkylamino, cyano, nitro, haloalkyl, and
- ii) alkyl, alkenyl, alkynyl, cycloalkyl, and (cycloalkyl)alkyl, each of which may be unsubstituted or substituted by one or more of halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkoxy, amino, and mono- or dialkylamino;

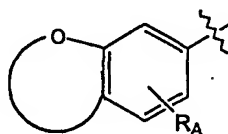
R₄ is hydrogen or

alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl, haloalkyl, each of which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino and mono- or dialkylamino,

R₄ is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenylalkyl, chromanyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl,

oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, indanyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinoliny, isoquinoliny, cinnoliny, quinazoliny, or quinoxaliny, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino, mono- or dialkylamino, aminoalkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or dialkylaminocarbonyl, N-alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl and -X₄R_B, wherein X₄ and R_B are as defined below; or

R₄ is a bicyclic oxygen-containing group of the formula:



wherein R_A represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino, and mono- or dialkylamino;

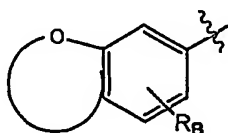
Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently chosen from

- i) phenyl, phenylalkyl, chromanyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, indanyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinoliny, isoquinoliny, cinnoliny, quinazoliny, or quinoxaliny, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino, mono- or

dialkylamino, aminoalkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or dialkylaminocarbonyl, N-alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl and -X₄R_B, wherein X₄ and R_B are as defined below;, and

ii) bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkyl, alkenyl, alkynyl, alkoxy, amino, and mono- or dialkylamino;

X₄ is independently selected at each occurrence from the group consisting of -CH₂-, -CHR_C-, -O-, -S(O)_m-, -NH-, -NR_C-, -C(=O)NH-, -C(=O)NR_C-, -S(O)_mNH-, -S(O)_mNR_C-, -NHC(=O)-, -NR_CC(=O)-, -NHS(O)_m-, -C(=O)NHS(O)_m-, and -NR_CS(O)_m- (where m is 0, 1, or 2); and

R_B and R_C, which may be the same or different, are independently selected at each occurrence from the group consisting of:

hydrogen, straight, branched, or cyclic alkyl groups, which may contain one or more double or triple bonds, each of which may unsubstituted or substituted with one or more substituent(s) selected from:

oxo, hydroxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(alkyl), -N(alkyl)C(O)(alkyl), -NHS(O)_x(alkyl), -S(O)_x(alkyl), -S(O)_xNH(alkyl), -S(O)_xN(alkyl)(alkyl), (where x is 0, 1, or 2).

88. A compound according to Claim 86, wherein:

R is selected from

i) hydrogen, halogen, hydroxy, amino, C₁-C₆ alkoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, haloalkyl, and

- ii) C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, and (C₃-C₈)cycloalkyl) C₁-C₃ alkyl, each of which may be unsubstituted or substituted by one or more of halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkoxy, amino, and mono- or di(C₁-C₆)alkylamino,
- iii) phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino;

R₂ and R₃ are independently selected from

- i) hydrogen, halogen, hydroxy, amino, C₁-C₆ alkoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, haloalkyl, and
- ii) C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, and (C₃-C₈ cycloalkyl) C₁-C₃ alkyl, each of which may be unsubstituted or substituted by one or more of halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino;

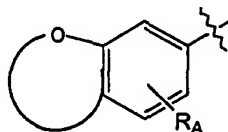
R₄ is hydrogen or

C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈cycloalkyl, (C₃₋₈ cycloalkyl)C₁₋₄alkyl, haloalkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino,

R₄ is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenylalkyl, chromanyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, indanyl, isoindolyl,

benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinoliny, isoquinoliny, cinnoliny, quinazoliny, or quinoxaliny, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidiny, 1-piperidyl, -X₄R_B, wherein X₄ and R_B are as defined below; or

R₄ is a bicyclic oxygen-containing group of the formula:



wherein R_A represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino;

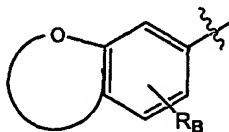
Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently chosen from

- i) phenyl, phenylalkyl, chromanyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, indanyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, quinoliny, isoquinoliny, cinnoliny, quinazoliny, or quinoxaliny, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of

carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl, and -X₄R_B, wherein X₄ and R_B are as defined below; and

ii) bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino;

X₄ is independently selected at each occurrence from the group consisting of -CH₂-, -CHR_C-, -O-, -S(O)_m-, -NH-, -NR_C-, -C(=O)NH-, -C(=O)NR_C-, -S(O)_mNH-, -S(O)_mNR_C-, -NHC(=O)-, -NR_CC(=O)-, -NHS(O)_m-, -C(=O)NHS(O)_m-, and -NR_CS(O)_m- (where m is 0, 1, or 2); and

R_B and R_C, which may be the same or different, are independently selected at each occurrence from the group consisting of:

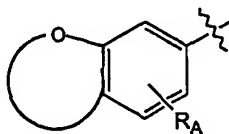
hydrogen, straight, branched, or cyclic alkyl groups, which may contain one or more double or triple bonds, each of which may unsubstituted or substituted with one or more substituent(s) selected from:

oxo, hydroxy, -O(C₁-C₆ alkyl), -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)(C₁-C₆ alkyl), -NHC(O)(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)C(O)(C₁-C₆ alkyl), -NHS(O)_x(C₁-C₆ alkyl), -S(O)_x(C₁-C₆ alkyl), -S(O)_xNH(C₁-C₆ alkyl), -S(O)_xN(C₁-C₆ alkyl)(C₁-C₆ alkyl), (where x is 0, 1, or 2).

89. A compound according to Claim 86, wherein:

R is hydrogen, halogen, hydroxy, C₁-C₆ alkoxy, haloalkyl, C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, and (C₃-C₈)cycloalkyl C₁-C₃ alkyl, or

- R is phenyl substituted with up to five groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino, aminocarbonyl, sulfonamido, mono or di(C₁-C₆)alkylsulfonamido, 3,4-methylenedioxy, and 3,4-(1,2-ethylene)dioxy;
- R₂ is selected from C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, (C₃-C₈ cycloalkyl) C₁-C₃ alkyl and haloalkyl;
- R₃ is hydrogen C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl;
- R₄ is C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈cycloalkyl, (C₃₋₈ cycloalkyl)C₁₋₄alkyl, haloalkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino,
- R₄ is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, each of which may be substituted with up to five groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl,
- R₄ is a bicyclic oxygen-containing group of the formula:



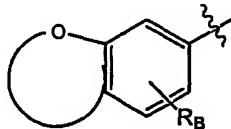
wherein R_A represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl,

C₂₋₆ alkenyl, C₂₋₆ alkynyl, C_{1-C6} alkoxy, amino, and mono- or di(C_{1-C6})alkylamino;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently chosen from

- i) phenyl, phenyl(C_{1-C4})alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, and benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_{1-C6} alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C_{1-C6} alkoxy, amino, mono- or di(C_{1-C6})alkylamino, amino(C_{1-C6})alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C_{1-C6})alkylaminocarbonyl, N-(C_{1-C6})alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidiny, 1-piperidyl; or
- ii) bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_{1-C6} alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C_{1-C6} alkoxy, amino, and mono- or di(C_{1-C6})alkylamino.

90. A compound according to Claim 89, wherein

R, R₂, R₃, R₄, and Ar₂ are as defined in Claim 89;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or phenyl with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_{1-C6} alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C_{1-C6} alkoxy, amino, mono- or di(C_{1-C6})alkylamino, and amino(C_{1-C6})alkoxy.

91. A compound according to Claim 89, wherein:

R, R₂, and R₃ are as defined in Claim 89;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or phenyl with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, and amino(C₁-C₆)alkoxy;

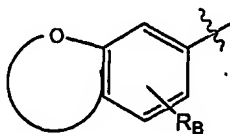
R₄ is C₃-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₃-C₈cycloalkyl, (C₃₋₈ cycloalkyl)C₁-C₄alkyl, C₁-C₈ haloalkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino,

R₄ is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidyl, 1-pyrrolidyl, 1-piperidyl;

Ar₂ is phenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, or benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-

C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidiny, 1-piperidyl; or

Ar₂ is bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino.

92. A compound according to Claim 89, wherein:

R is hydrogen, C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, or (C₃-C₈)cycloalkyl) C₁-C₃ alkyl, or

R is phenyl substituted with up to five groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino, aminocarbonyl, sulfonamido, mono or di(C₁-C₆)alkylsulfonamido, 3,4-methylenedioxy, and 3,4-(1,2-ethylene)dioxy;

R₂ is C₃-C₆ alkyl;

R₃ is hydrogen, methyl, or ethyl;

R₄ is C₃-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₃-C₈cycloalkyl, (C₃₋₈ cycloalkyl)C₁-C₄alkyl, C₁-C₈ haloalkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino,

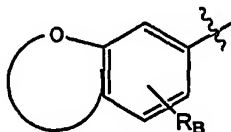
R₄ is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl,

benzodioxolyl, benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or phenyl with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, and amino(C₁-C₆)alkoxy;

Ar₂ is phenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, or benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl; or

Ar₂ is bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino.

93. A compound according to Claim 89, wherein:

R is hydrogen, C₁-C₈ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, or (C₃-C₈)cycloalkyl, C₁-C₃ alkyl, or phenyl;

R₂ is C₃-C₆ alkyl;

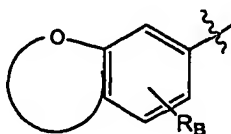
R₃ is hydrogen, methyl, or ethyl;

R₄ is C₃-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₃-C₈cycloalkyl, (C₃-C₈ cycloalkyl)C₁-C₄alkyl, C₁-C₈ haloalkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or phenyl with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, and amino(C₁-C₆)alkoxy; and

Ar₂ is phenyl, phenyl(C₁-C₄)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, or benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl; or

Ar₂ is bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_1 - C_6 alkoxy, amino, and mono- or di(C_1 - C_6)alkylamino.

94. A compound according to Claim 89, wherein:

R is hydrogen, C_1 - C_8 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_8 cycloalkyl, or (C_3 - C_8)cycloalkyl) C_1 - C_3 alkyl, or phenyl;

R_2 is C_3 - C_6 alkyl;

R_3 is hydrogen, methyl, or ethyl;

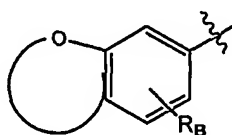
R_4 is phenyl, ethylenedioxyphenyl, methylenedioxyphenyl, phenyl(C_1 - C_4)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_1 - C_6 alkoxy, amino, mono- or di(C_1 - C_6)alkylamino, amino(C_1 - C_6)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C_1 - C_6)alkylaminocarbonyl, N-(C_1 - C_6)alkylsulfonylaminocarbonyl, 1-azetidyl, 1-pyrrolidinyl, 1-piperidyl;

Ar_1 is ethylenedioxyphenyl, methylenedioxyphenyl, or phenyl with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_1 - C_6 alkoxy, amino, mono- or di(C_1 - C_6)alkylamino, and amino(C_1 - C_6)alkoxy;

Ar_2 is phenyl, phenyl(C_1 - C_4)alkyl, thienyl, pyridyl, pyrimidyl, pyrazinyl, chromanyl, dihydrobenzofuranyl, naphthyl, indolyl, indanyl, benzo[b]thiophenyl, benzodioxanyl, benzodioxinyl, benzodioxolyl, or benz[d]isoxazolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_{2-6} alkenyl, C_{2-6}

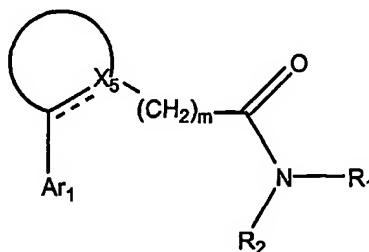
alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, 1-piperidyl; or

Ar₂ is bicyclic oxygen-containing groups of the formula:



wherein R_B represents 0 to 3 groups selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino.

95. A compound according to Claim 1 of the formula



or a pharmaceutically acceptable salt, prodrug or hydrate thereof, wherein:

X₅ is C, N or CH;

m is 0, 1, 2, or 3;

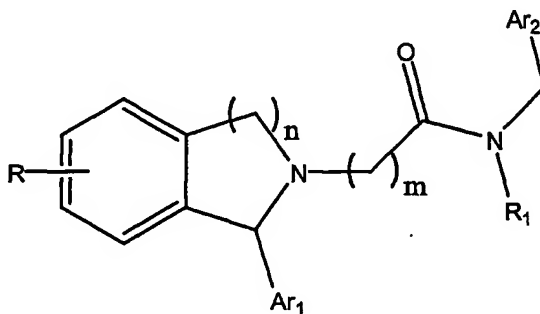
Ar₁ is chosen from optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms; and

R₁ and R₂ are independently chosen from C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈ cycloalkyl, (C₃₋₈ cycloalkyl)C₁₋₄alkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆

alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C_{1-C6} alkoxy, amino and mono- or di(C_{1-C6})alkylamino, or

R₁ and R₂ are independently chosen from phenyl, phenylalkyl, chromanyl, chromanylalkyl, imidazolyl, imidazolylalkyl, pyridyl, pyridylalkyl, pyrimidyl, pyrimidylalkyl, pyrazinyl, pyrazinylalkyl, indolyl, indolylalkyl, indanyl, indanylalkyl, imidazopyridyl, azaimidazopyridyl, benzimidazolyl, benzimidazolylalkyl, benzodioxolylalkyl, or benzodioxolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_{1-C6} alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C_{1-C6} alkoxy, amino, mono- or di(C_{1-C6})alkylamino, amino(C_{1-C6})alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C_{1-C6})alkylaminocarbonyl, N-(C_{1-C6})alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, and 1-piperidyl;

96. A compound according to Claim 95 of the formula:




or a pharmaceutically acceptable salt thereof, wherein:

R₁ is as defined in Claim 95;

m is 1, 2, or 3;

n is 1, 2, or 3;

 represents a carbon chain that may be substituted with hydrogen, halogen, cyano, nitro amino, mono or dialkyl amino, alkenyl, alkynyl, alkoxy,

trifluoromethyl, trifluoromethoxy, straight or branched chain alkyl, or cycloalkyl;

Ar₁ and Ar₂ independently optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or heteroalicyclic group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms; and

R represents up to 4 groups independently chosen from hydrogen, halogen, hydroxy, amino, alkoxy, acetoxy, mono- or dialkylamino, cyano, nitro, haloalkyl, alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl, hydroxy carbonyl (COOH), aminocarbonyl (CONH₂), mono or dialkylaminocarbonyl, sulfonamido, and mono or dialkylsulfonamido.

97. A compound according to Claim 96, wherein the compound exhibits an IC₅₀ of 1μM or less in an assay of C5a mediated chemotaxis or calcium mobilization.

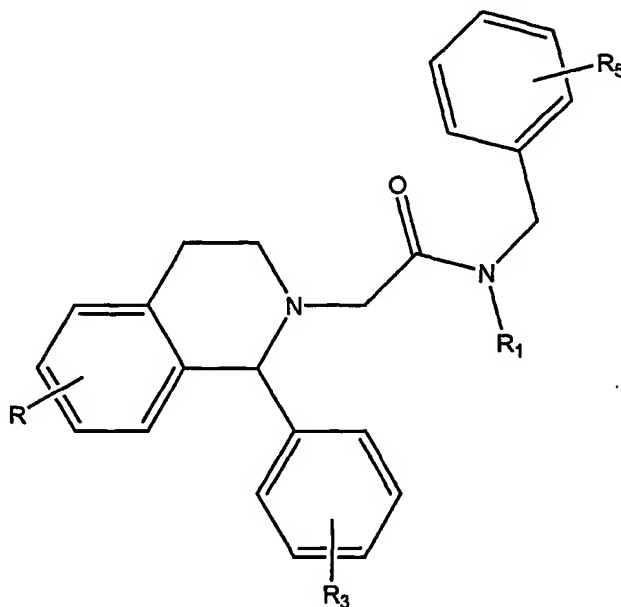
98. A compound according to Claim 96, wherein
n, m, and R₁ are defined as in Claim 96;

Ar₁ is independently chosen from phenyl, pyridyl, and pyrimidinyl each of which is optionally optionally substituted or substituted with up to 4 groups independently chosen from hydrogen, halogen, hydroxy, amino, C₁-C₆ alkoxy, acetoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, C₁-C₆ haloalkyl, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, (C₃-C₈cycloalkyl) C₁-C₃alkyl, hydroxy carbonyl (COOH), aminocarbonyl (CONH₂), mono or di(C₁-C₆)alkylaminocarbonyl, sulfonamido, 3,4-methylenedioxy, ethylenedioxy, and mono or di(C₁-C₆)alkylsulfonamido; and

Ar₂ represents suberanyl, indanyl, tetrahydronaphtyl, or indolyl, each of which is optionally optionally substituted or substituted with up to 4 groups independently chosen from hydrogen, halogen, hydroxy, amino, C₁-C₆ alkoxy, acetoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, C₁-C₆ haloalkyl,

C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, (C₃-C₈cycloalkyl) C₁-C₃alkyl, hydroxy carbonyl (COOH), aminocarbonyl (CONH₂), mono or di(C₁-C₆)alkylaminocarbonyl, sulfonamido, 3,4-methylenedioxy, ethylenedioxy, and mono or di(C₁-C₆)alkylsulfonamido.

99. A compound according to Claim 95 of the formula



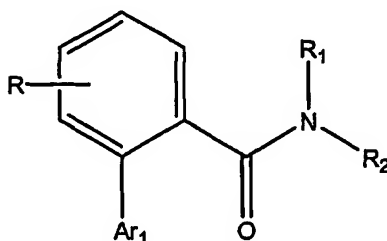
R, R₃, and R₅ each represent up to 5 groups independently chosen from hydrogen, halogen, hydroxy, amino, C₁-C₆ alkoxy, acetoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, C₁-C₆ haloalkyl, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, (C₃-C₈cycloalkyl) C₁-C₃alkyl, hydroxy carbonyl (COOH), aminocarbonyl (CONH₂), mono or di(C₁-C₆)alkylaminocarbonyl, sulfonamido, and mono or di(C₁-C₆)alkylsulfonamido; and represents suberanyl, indanyl, tetrahydronaphthyl, or indolyl, each of which is optionally optionally substituted or substituted with up to 4 groups independently chosen from hydrogen, halogen, hydroxy, amino, C₁-C₆ alkoxy, acetoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, C₁-C₆ haloalkyl, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, (C₃-C₈cycloalkyl) C₁-C₃alkyl, hydroxy carbonyl (COOH), aminocarbonyl (CONH₂), mono or di(C₁-

C₆)alkylaminocarbonyl, sulfonamido, 3,4-methylenedioxy, ethylenedioxy, and mono or di(C₁-C₆)alkylsulfonamido.

R₁ is chosen from C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈cycloalkyl, (C₃₋₈ cycloalkyl)C₁₋₄alkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino, or

R₁ is chosen from phenyl, phenylalkyl, chromanyl, chromanylalkyl, imidazolyl, imidazolylalkyl, pyridyl, pyridylalkyl, pyrimidyl, pyrimidylalkyl, pyrazinyl, pyrazinylalkyl, indolyl, indolylalkyl, indanyl, indanylalkyl, imidazopyridyl, azaimidazopyridyl, benzimidazolyl, benzimidazolylalkylbenzodioxolylalkyl, or benzodioxolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, and 1-piperidyl;

100. A compound according to Claim 95 of the formula:



or a pharmaceutically acceptable salt or prodrug, thereof, wherein:

R represents up to 4 groups independently chosen from hydrogen, halogen, hydroxy, amino, alkoxy, acetoxy, mono- or dialkylamino, cyano, nitro, haloalkyl, alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl, hydroxy carbonyl (COOH),

aminocarbonyl (CONH₂), mono or di(C₁-C₆)alkylaminocarbonyl, sulfonamido, 3,4-methylenedioxy, ethylenedioxy, and mono or dialkylsulfonamido;

R₁ and R₂ are independently chosen from C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈cycloalkyl, (C₃₋₈ cycloalkyl)C₁₋₄alkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino, or

R₁ and R₂ are independently chosen from phenyl, phenylalkyl, chromanyl, chromanylalkyl, imidazolyl, imidazolylalkyl, pyridyl, pyridylalkyl, pyrimidyl, pyrimidylalkyl, pyrazinyl, pyrazinylalkyl, indolyl, indolylalkyl, indanyl, indanylalkyl, imidazopyridyl, azaimidazopyridyl, benzimidazolyl, benzimidazolylalkyl, benzodioxolylalkyl, or benzodioxolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, and 1-piperidyl;

Ar₁ is chosen from optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, or an optionally substituted heteroalicyclic, heteroalicyclicalkyl group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms, ethylenedioxyphenyl or methylenedioxyphenyl.

101. A compound according to Claim 100, wherein the compound exhibits an IC₅₀ of 1 μM or less in an assay of C5a mediated chemotaxis or calcium mobilization.

102. A compound according to Claim 100, wherein

R represents up to 4 groups independently chosen from hydrogen, halogen, hydroxy, amino, C₁-C₆ alkoxy, acetoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, C₁-C₆ haloalkyl, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, (C₃-C₈ cycloalkyl) C₁-C₃ alkyl, hydroxy carbonyl (COOH), aminocarbonyl (CONH₂), mono or di(C₁-C₆)alkylaminocarbonyl, sulfonamido, 3,4-methylenedioxy, ethylenedioxy, and mono or di(C₁-C₆)alkylsulfonamido;

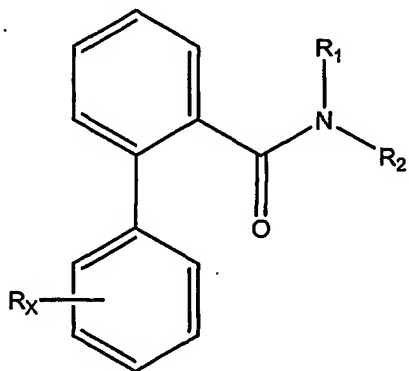
R₁ and R₂ are independently chosen from C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈ cycloalkyl, (C₃₋₈ cycloalkyl)C₁₋₄alkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino, or

R₁ and R₂ are independently chosen from phenyl, phenylalkyl, chromanyl, chromanylalkyl, imidazolyl, imidazolylalkyl, pyridyl, pyridylalkyl, pyrimidyl, pyrimidylalkyl, pyrazinyl, pyrazinylalkyl, indolyl, indolylalkyl, indanyl, indanylalkyl, imidazopyridyl, azaimidazopyridyl, benzimidazolyl, benzimidazolylalkyl, benzodioxolylalkyl, or benzodioxolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, and 1-piperidyl;

Ar₁ is chosen from ethylenedioxyphenyl, methylenedioxyphenyl, phenyl, pyrrolyl, imidazolyl, pyrazolyl, triazolyl, thiophenyl, and pyridyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy,

haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino, amino(C₁-C₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁-C₆)alkylaminocarbonyl, and N-(C₁-C₆)alkylsulfonylaminocarbonyl; and

103. A compound according to Claim 102, of the formula



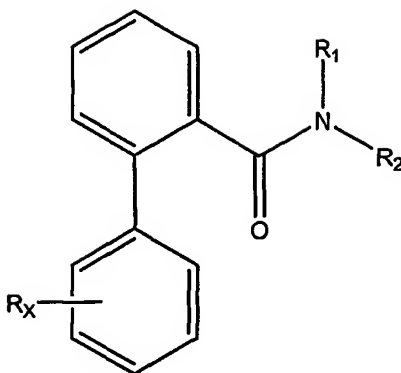
wherein:

R₂ is as defined in Claim 102;

R_x represents up to 5 groups independently chosen from hydrogen, halogen, hydroxy, amino, C₁-C₆ alkoxy, acetoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, C₁-C₆ haloalkyl, C₁-C₆ alkyl, C₂-C₆ alkenyl, and C₂-C₆ alkynyl; and

R₁ is C₁-C₆alkyl, C₃-C₈cycloalkyl, (C₃-C₈ cycloalkyl)C₁-C₄alkyl, phenyl, phenylC₁-C₆alkyl, chromanyl, chromanylC₁-C₆alkyl, imidazolyl, imidazolylC₁-C₆alkyl, pyridyl, pyridylC₁-C₆alkyl, pyrimidyl, pyrimidylC₁-C₆alkyl, pyrazinyl, pyrazinylC₁-C₆alkyl, indolyl, indolylC₁-C₆alkyl, indanyl, indanylC₁-C₆alkyl, benzodioxolyl, or benzodioxolylC₁-C₆alkyl each or which may be unsubstituted or substituted with up to 4 substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino.

104. A compound according to Claim 102, of the formula:



wherein:

R_X represents up to 4 groups independently chosen from hydrogen, halogen, hydroxy, amino, C₁-C₆ alkoxy substituted with 0-2 R₂, acetoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, C₁-C₆ haloalkyl, C₁-C₆ alkyl, C₂-C₆ alkenyl, and C₂-C₆ alkynyl;

R₁ is phenyl, phenylC₁-C₆ alkyl, C₃-C₈ cycloalkyl, C₃-C₈ cycloalkyl(C₁-C₄ alkyl), naphthyl, naphthylC₁-C₆alkyl, indanyl, indanylC₁-C₆ alkyl, benzodioxolanyl, or benzodioxolanylC₁-C₆ alkyl, each of which may be substituted by up to 4 groups chosen from halogen, hydroxy, amino, C₁-C₆ alkoxy, acetoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, C₁-C₆ haloalkyl, C₁-C₆ alkyl; and

R₂ is chosen from C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈cycloalkyl, (C₃₋₈ cycloalkyl)C₁₋₄alkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino, or

R₂ is chosen from phenyl, phenylalkyl, chromanyl, chromanylalkyl, imidazolyl, imidazolylalkyl, pyridyl, pyridylalkyl, pyrimidyl, pyrimdylalkyl, pyrazinyl, pyrazinylalkyl, indolyl, indolylalkyl, indanyl, indanylalkyl, imidazopyridyl, azaimidazopyridyl, benzimidazolyl, benzimidazolylalkylbenzodioxolylalkyl, or benzodioxolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl,

C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, amino, mono- or di(C₁₋₆)alkylamino, amino(C₁₋₆)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C₁₋₆)alkylaminocarbonyl, N-(C₁₋₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidiny, and 1-piperidyl;

105. A compound according to Claim 102 wherein:

R₂ is as defined in Claim 102;

R represents up to 4 groups independently chosen from hydrogen, halogen, amino,

C₁₋₆ alkoxy, C₁₋₆ alkyl, trifluoromethyl, and trifluoromethoxy;

R₁ is phenyl, benzyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkyl(C₁₋₄ alkyl), naphthyl,

naphthyl-CH₂-, indanyl, indandyl-CH₂-, benzodioxolanyl-CH₂-, or

benzodioxolanyl, each of which may be substituted by up to 4 groups chosen from halogen, hydroxy, amino, C₁₋₆ alkoxy, acetoxy, mono- or di(C₁₋

C₆)alkylamino, cyano, nitro, C₁₋₆ haloalkyl, C₁₋₆ alkyl; and

Ar₁ is chosen from ethylenedioxyphenyl, methylenedioxyphenyl, pyrrolyl, imidazolyl, pyrazolyl, triazolyl, thiophenyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, trifluoromethyl, trifluoromethoxy, C₁₋₆ alkoxy, C₁₋₆ alkyl, and amino.

106. A compound according to Claim 102 wherein:

R represents up to 4 groups independently chosen from hydrogen, halogen, amino,

C₁₋₆ alkoxy, C₁₋₆ alkyl, trifluoromethyl, and trifluoromethoxy;

R₁ is benzyl which is unsubstituted or substituted by up to 4 groups chosen from

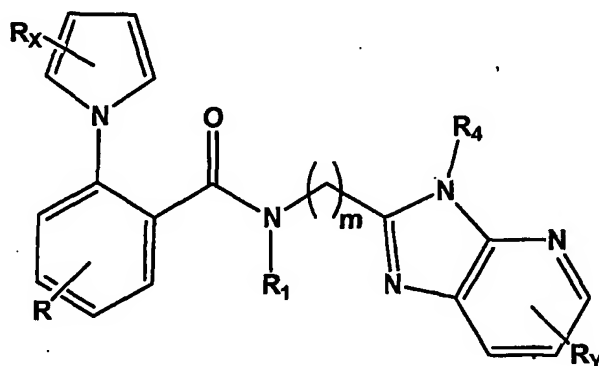
halogen, hydroxy, amino, C₁₋₆ alkoxy, acetoxy, mono- or di(C₁₋

C₆)alkylamino, cyano, nitro, C₁₋₆ haloalkyl, C₁₋₆ alkyl;

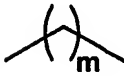
Ar₁ is chosen from ethylenedioxyphenyl, methylenedioxyphenyl, pyrrolyl, imidazolyl, pyrazolyl, triazolyl, thiophenyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, trifluoromethyl, trifluoromethoxy, C₁₋₆ alkoxy, C₁₋₆ alkyl, and amino; and

R_2 is chosen from phenyl, benzyl, indolyl, indolyl-CH₂-, indanyl, indanyl-CH₂-, chromanyl, chromanyl-CH₂-, benzofuranyl, benzofuranyl-CH₂-, benzodioxinyl, benzodioxinyl-CH₂-, benzodioxolyl-CH₂-, and benzodioxolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from: halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, and mono- or di(C₁-C₆)alkylamino.

107. A compound according to Claim 102, of the Formula

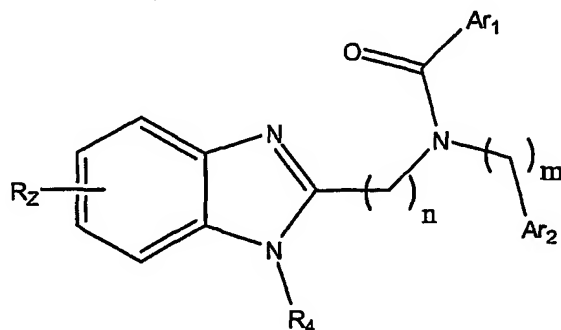


wherein:

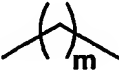
m is 0, 1, 2, or 3, and  represents a carbon chain which is optionally substituted with methyl, ethyl, methoxy, ethoxy, hydroxy, halogen, or amino; R represents up to 4 groups independently chosen from hydrogen, halogen, hydroxy, amino, C₁-C₆alkyl, C₂-C₆ alkenyl, C₁-C₆alkynyl, C₁-C₆ alkoxy, acetoxy, mono- or di(C₁-C₆)alkylamino; R_X and R_Y each represent up to 4 groups independently chosen from hydrogen, halogen, hydroxy, amino, C₁-C₆ alkoxy, acetoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, C₁-C₆ haloalkyl, C₁-C₆ alkyl, C₂-C₆ alkenyl, and C₂-C₆ alkynyl; and R_1 and R_4 are independently selected from C₁-C₆alkyl, C₃-C₈cycloalkyl, (C₃-C₈ cycloalkyl)C₁-C₄alkyl, phenyl, phenylC₁-C₆alkyl, pyridyl, and pyridylC₁-

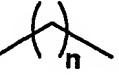
C₆alkyl, each or which may be unsubstituted or substituted with up to 4 substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁-C₆ alkoxy, amino and mono- or di(C₁-C₆)alkylamino.

108. A compound according to Claim 1 of the formula



or a pharmaceutically acceptable salt, prodrug or hydrate thereof, wherein;

m is 0, 1, 2, or 3, and  represents a carbon chain which is optionally substituted with methyl, ethyl, methoxy, ethoxy, hydroxy, halogen, or amino;

n is 0, 1, 2, or 3, and  represents a carbon chain which is optionally substituted with methyl, ethyl, methoxy, ethoxy, hydroxy, halogen, or amino;

R₂ represents up to 4 groups independently chosen from hydrogen, halogen, hydroxy, amino, alkoxy, acetoxy, mono- or dialkylamino, cyano, nitro, haloalkyl, alkyl, alkenyl, alkynyl, cycloalkyl, and (cycloalkyl)alkyl;

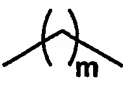
R₄ is chosen from alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl) alkyl, aryl and arylalkyl, each of which may be unsubstituted, optionally substituted or substituted by one or more of halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, alkoxy, amino, mono- or dialkylamino; and

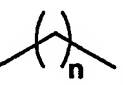
Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, optionally substituted heteroarylalkyl, or an optionally substituted heteroalicyclic or heteroalicyclicalkyl group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms.

109. A compound according to Claim 108, wherein the compound exhibits an IC₅₀ of 1μM or less in an assay of C5a mediated chemotaxis or calcium mobilization.

110. A compound according to Claim 108, wherein

m is 1 and  represents a carbon chain which is unsubstituted;

n is 1 and  represents a carbon chain which is unsubstituted;

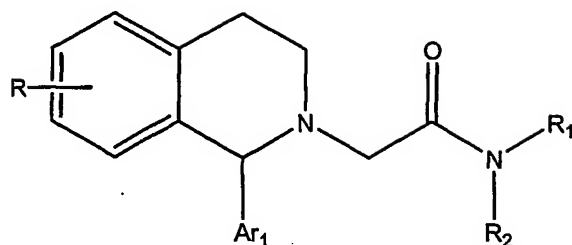
R represents up to 4 groups independently chosen from hydrogen, halogen, hydroxy, amino, C₁-C₆ alkoxy, acetoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, C₁-C₆ haloalkyl, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₂-C₆ cycloalkyl, and(C₃-C₈ cycloalkyl) C₁-C₄ alkyl;

R₂ is C₃-C₈ alkyl or C₃-C₈ cycloalkyl;

Ar₁ is ethylenedioxyphenyl, methylenedioxyphenyl, or;

Ar₁ and Ar₂ are independently chosen from phenyl, phenyl(C₁-C₄)alkyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, pyridyl, pyrimidyl, and pyrazinyl, each of which may be unsubstituted or optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, amino, mono- or di(C₁-C₆)alkylamino.

111. A compound according to Claim 95 of the formula

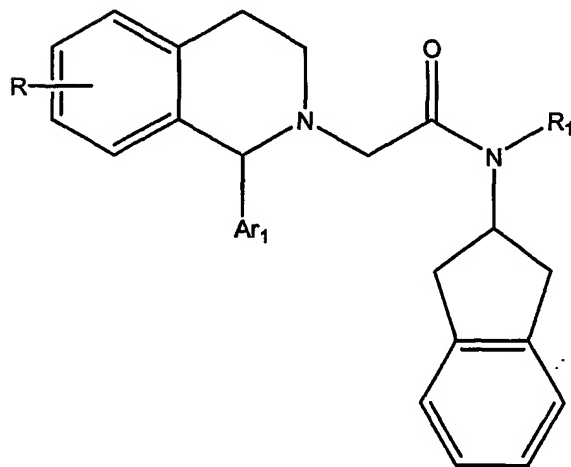


wherein:

Ar₁, R₁ and R₂ are as defined in Claim 95; and

R represents up to 4 groups independently chosen from hydrogen, halogen, hydroxy, amino, C₁-C₆ alkoxy, acetoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, C₁-C₆ haloalkyl, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, (C₃-C₈ cycloalkyl) C₁-C₃ alkyl, hydroxy carbonyl (COOH), aminocarbonyl (CONH₂), mono or di(C₁-C₆)alkylaminocarbonyl, sulfonamido, 3,4-methylenedioxy, ethylenedioxy, and mono or di(C₁-C₆)alkylsulfonamido;

112. A compound according to Claim 95 of the formula



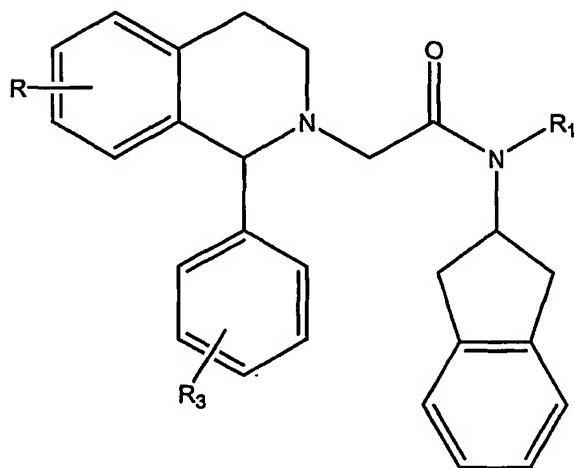
wherein:

Ar₁ and R₁ are as defined in Claim 95; and

R represents up to 4 groups independently chosen from hydrogen, halogen, hydroxy, amino, C₁-C₆ alkoxy, acetoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, C₁-C₆ haloalkyl, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, (C₃-C₈ cycloalkyl) C₁-C₃ alkyl, hydroxy carbonyl (COOH), aminocarbonyl (CONH₂),

mono or di(C₁-C₆)alkylaminocarbonyl, sulfonamido, 3,4-methylenedioxy, ethylenedioxy, and mono or di(C₁-C₆)alkylsulfonamido;

113. A compound according to Claim 95 of the formula

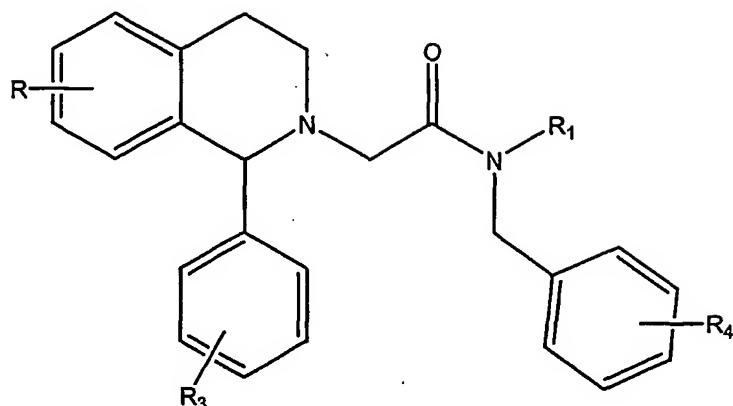


wherein:

R₁ is as defined in Claim 95; and

R and R₃ represent up to 5 groups independently chosen from hydrogen, halogen, hydroxy, amino, C₁-C₆ alkoxy, acetoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, C₁-C₆ haloalkyl, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, (C₃-C₈ cycloalkyl) C₁-C₃ alkyl, hydroxy carbonyl (COOH), aminocarbonyl (CONH₂), mono or di(C₁-C₆)alkylaminocarbonyl, sulfonamido, 3,4-methylenedioxy, ethylenedioxy, and mono or di(C₁-C₆)alkylsulfonamido;

114. A compound according to Claim 95 of the formula



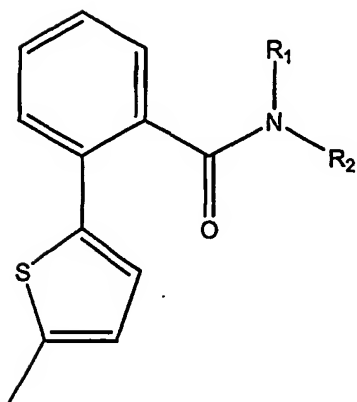
wherein:

R₁ is as defined in Claim 95; and

R, R₃ and R₄ represent up to 5 groups independently chosen from hydrogen,

halogen, hydroxy, amino, C₁-C₆ alkoxy, acetoxy, mono- or di(C₁-C₆)alkylamino, cyano, nitro, C₁-C₆ haloalkyl, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, (C₃-C₈ cycloalkyl) C₁-C₃ alkyl, hydroxy carbonyl (COOH), aminocarbonyl (CONH₂), mono or di(C₁-C₆)alkylaminocarbonyl, sulfonamido, 3,4-methylenedioxy, ethylenedioxy, and mono or di(C₁-C₆)alkylsulfonamido;

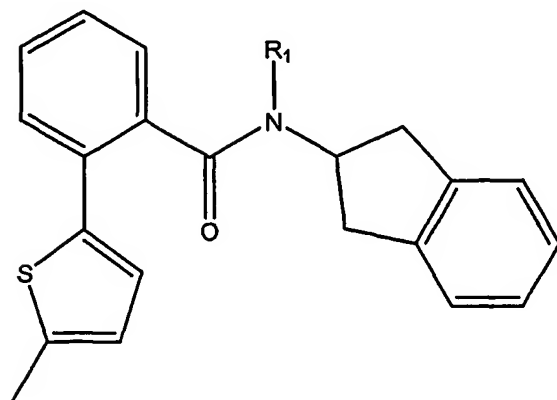
115. A compound according to Claim 95 of the formula



wherein:

R₁ and R₂ are as defined in Claim 95.

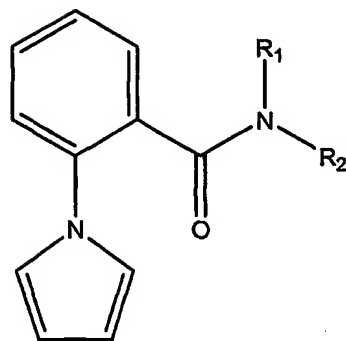
116. A compound according to Claim 95 of the formula



wherein:

R₁ is as defined in Claim 95.

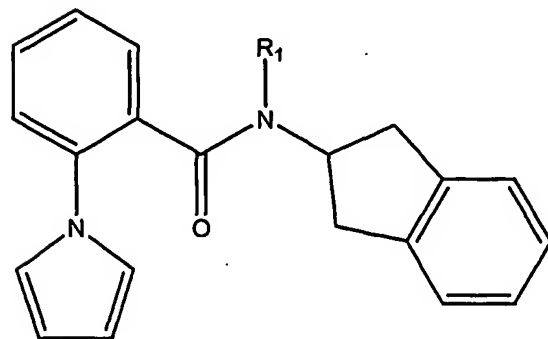
117. A compound according to Claim 95 of the formula



wherein:

R₁ and R₂ are as defined in Claim 95.

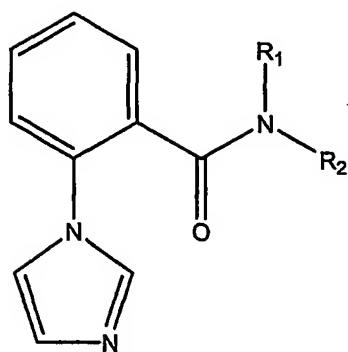
118. A compound according to Claim 95 of the formula



wherein:

R₁ is as defined in Claim 95.

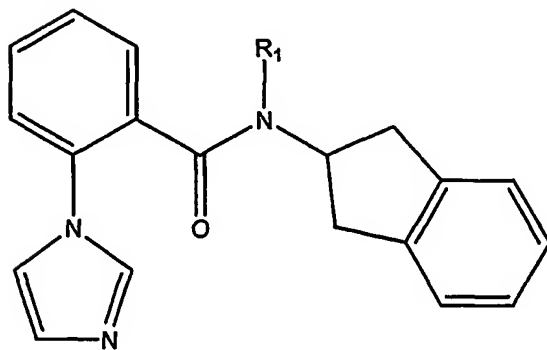
119. A compound according to Claim 95 of the formula



wherein:

R₁ and R₂ are as defined in Claim 95.

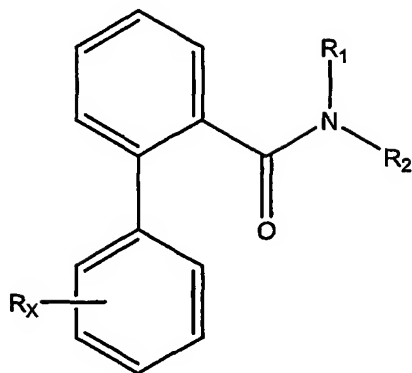
120. A compound according to Claim 95 of the formula



wherein:

R₁ is as defined in Claim 95.

121. A compound according to Claim 95 of the formula

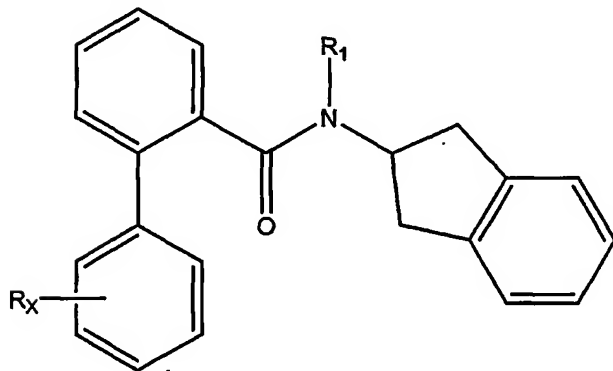


wherein:

R_1 and R_2 are as defined in Claim 95; and

R_X represents up to 5 groups independently chosen from hydrogen, halogen, hydroxy, amino, C_1 - C_6 alkoxy, acetoxy, mono- or di(C_1 - C_6)alkylamino, cyano, nitro, C_1 - C_6 haloalkyl, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, and C_2 - C_6 alkynyl.

122. A compound according to Claim 95 of the formula

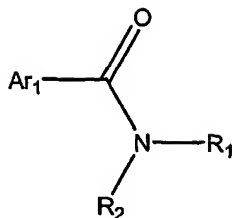


wherein:

R_1 is as defined in Claim 95; and

R_X represents up to 5 groups independently chosen from hydrogen, halogen, hydroxy, amino, C_1 - C_6 alkoxy, acetoxy, mono- or di(C_1 - C_6)alkylamino, cyano, nitro, C_1 - C_6 haloalkyl, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, and C_2 - C_6 alkynyl.

123. A compound according to Claim 1 of the formula



wherein

R_1 and R_2 are independently chosen from C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, $(C_{3-8}$ cycloalkyl) C_{1-4} alkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_1 - C_6 alkoxy, amino and mono- or di(C_1 - C_6)alkylamino, or

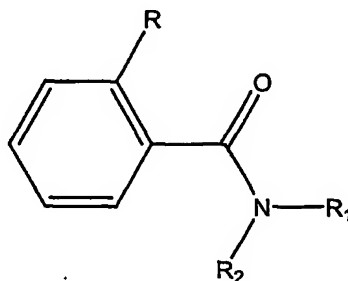
R_1 and R_2 are independently chosen from phenyl, phenylalkyl, chromanyl, chromanylalkyl, imidazolyl, imidazolylalkyl, pyridyl, pyridylalkyl, pyrimidyl, pyrimidylalkyl, pyrazinyl, pyrazinylalkyl, indolyl, indolylalkyl, indanyl, indanylalkyl, imidazopyridyl, azaimidazopyridyl, benzimidazolyl, benzimidazolylalkyl, benzodioxolylalkyl, or benzodioxolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_1 - C_6 alkoxy, amino, mono- or di(C_1 - C_6)alkylamino, amino(C_1 - C_6)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C_1 - C_6)alkylaminocarbonyl, N-(C_1 - C_6)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, and 1-piperidyl;

Ar_1 is chosen from optionally substituted carbocyclic aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, or an optionally substituted heteroalicyclic, heteroalicyclicalkyl group having from 1 to 3 rings, 3 to 8 members in each ring and from 1 to 3 heteroatoms, ethylenedioxyphenyl or methylenedioxyphenyl; and

124. A compound according to Claim 123 wherein

R_1 and R_2 are connected to form a 5-8 member optionally substituted carbocyclic or heterocyclic ring.

125. A compound according to Claim 123 of the formula



wherein

R_1 and R_2 are independently chosen from C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, $(C_{3-8}$ cycloalkyl) C_{1-4} alkyl, each or which may be unsubstituted or substituted with one or more substituents selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_1 - C_6 alkoxy, amino and mono- or di(C_1 - C_6)alkylamino, or

R_1 and R_2 are independently chosen from phenyl, phenylalkyl, chromanyl, chromanylalkyl, imidazolyl, imidazolylalkyl, pyridyl, pyridylalkyl, pyrimidyl, pyrimidylalkyl, pyrazinyl, pyrazinylalkyl, indolyl, indolylalkyl, indanyl, indanylalkyl, imidazopyridyl, azaimidazopyridyl, benzimidazolyl, benzimidazolylalkyl, benzodioxolylalkyl, or benzodioxolyl, each of which may be optionally substituted or substituted with up to four groups independently selected from halogen, nitro, cyano, trifluoromethyl, trifluoromethoxy, haloalkyl, hydroxy, acetoxy, C_1 - C_6 alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_1 - C_6 alkoxy, amino, mono- or di(C_1 - C_6)alkylamino, amino(C_1 - C_6)alkoxy, carboxylic acid, esters of carboxylic acids, aminocarbonyl, mono or di(C_1 -

C₆)alkylaminocarbonyl, N-(C₁-C₆)alkylsulfonylaminocarbonyl, 1-azetidiny, 1-pyrrolidinyl, and 1-piperidyl;

R is chosen from hydrogen, halogen, hydroxy, amino, alkoxy, acetoxy, mono- or dialkylamino, cyano, nitro, haloalkyl, alkyl, alkenyl, alkynyl, cycloalkyl, (cycloalkyl)alkyl, hydroxy carbonyl (COOH), aminocarbonyl (CONH₂), mono or di(C₁-C₆)alkylaminocarbonyl, sulfonamido, and mono or dialkylsulfonamido;

126. A compound according to Claim 125 wherein

R₁ and R₂ are connected to form a 5-8 member optionally substituted carbocyclic or heterocyclic ring.

127. A compound according to Claim 95 wherein:

Ar₁ is bound to the ring bearing X₅ to form an optionally substituted heterocyclic 5-8 member ring.

128. A compound according to Claim 95 wherein:

R₁ and R₂ are connected to form a 5-8 member optionally substituted carbocyclic or heterocyclic ring.

129. A compound according to Claim 95 wherein:

Ar₁ is bound to the ring bearing X₅ to form an optionally substituted heterocyclic 5-8 member ring; and

R₁ and R₂ are connected to form a 5-8 member optionally substituted carbocyclic or heterocyclic ring.

130. A compound according to Claim 5 wherein:

R₄ and Ar₂ are connected to form a 5-8 member optionally substituted carbocyclic or heterocyclic ring.

131. A compound according to Claim 8 wherein:

R₄ and Ar₂ are connected to form a 5-8 member optionally substituted carbocyclic or heterocyclic ring.

132. A compound according to Claim 3 wherein:

A has hydrogen bond acceptor ability.

133. A compound as set forth in any of Tables 1 through 6, or a pharmaceutically acceptable salt, prodrug or hydrate thereof.

134. A compound that is:

1-(1-butyl)-2-phenyl-5-(N,N-di[3,4-methylenedioxyphenylmethyl])aminomethylimidazole

1-(1-butyl)-2-phenyl-5-(1-[N-(3,4-methylenedioxyphenylmethyl)-N-phenylmethyl]amino)ethylimidazole

1-Butyl-2-phenyl-4-bromo-5-(N-phenylmethyl-N-[1-butyl])aminomethylimidazole

1-(1-Butyl)-2-phenyl-4-methyl-5-(N-[3,4-methylenedioxyphenyl-methyl]-N-phenylmethyl)aminomethylimidazole

1-(1-Butyl)-2-(4-fluorophenyl)-5-(N-[1,4-benzodioxan-6-yl]methyl-N-phenylmethyl) aminomethylimidazole

1-(1-Butyl)-2-(4-fluorophenyl)-5-(N-[3,4-methylenedioxyphenylmethyl]-N-phenylmethyl) aminomethylimidazole

1-(1-Butyl)-2-(4-fluorophenyl)-5-(N-[1,4-benzodioxan-6-yl]methyl-N-phenylmethyl) aminomethylimidazole

1-(1-Butyl)-2-(4-fluorophenyl)-5-(N-[3,4-methylenedioxyphenylmethyl]-N-phenylmethyl) aminomethylimidazole

1-(1-Butyl)-2-(2-fluorophenyl)-5-(N-[1,4-benzodioxan-6-ylmethyl]-N-phenylmethyl)amino- methylimidazole

1-(1-Butyl)-2-(2-methoxyphenyl)-5-(N-[naphtha-2-ylmethyl]-N-phenylmethyl)amino-methylimidazole

1-(1-Butyl)-2-(2-methoxyphenyl)-5-(N-[3,4-methylenedioxyphenylmethyl]-N-phenylmethyl) aminomethylimidazole

1-(1-Butyl)-2-(2-methoxyphenyl)-5-(N,N-di[3,4-methylenedioxyphenylmethyl]) aminomethylimidazole

1-(1-Butyl)-2-(2-methoxyphenyl)-5-(N-[4-dimethylaminophenylmethyl]-N-phenylmethyl) aminomethylimidazole

1-(1-Butyl)-2-(2-methylphenyl)-5-(N-[3,4-methylenedioxyphenylmethyl]-N-phenylmethyl) aminomethylimidazole

1-(1-Butyl)-2-(4-fluorophenyl)-5-(N,N-di[3,4-methylenedioxyphenylmethyl])amino- methylimidazole

1-(1-Butyl)-2-(2-methylphenyl)-5-(N,N-di[3,4-methylenedioxyphenylmethyl])amino- methylimidazole

1-(1-Butyl)-2-(3-fluorophenyl)-5-(N-[naphth-2-ylmethyl]-N-phenylmethyl)amino methylimidazole

1-(1-Butyl)-2-(3-fluorophenyl)-5-(N-[3,4-methylenedioxyphenylmethyl]-N-phenylmethyl) aminomethylimidazole

1-(1-Butyl)-2-(3-fluorophenyl)-5-(N,N-di[3,4-methylenedioxyphenylmethyl])amino- methylimidazole

1-(1-Butyl)-2-(3-methoxyphenyl)-5-(N-[3,4-methylenedioxyphenylmethyl]-N-phenylmethyl)- aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-{1-(N-[3,4-methylenedioxyphenylmethyl]-N-phenylmethyl)amino} ethylimidazole

1-(1-Pentyl)-2-phenyl-5-(N-[indol-5-ylmethyl]-N-phenylmethyl) aminomethylimidazole

1-(1-Propyl)-2-phenyl-5-(N-[indol-5-ylmethyl]-N-phenylmethyl) aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[1-(S)-phenylethyl]-N-phenylmethyl)aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[1-(R)-phenylethyl]-N-phenylmethyl)aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-[3,4-dichlorophenyl]methyl)aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N,N-di[3,4-methylenedioxyphenylmethyl])aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-[3,4-methoxyphenylmethyl])-aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-[4-(1-propyl)phenylmethyl])aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-[3,4-dichlorophenylethyl])aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenyl]methyl-N-[4-nitrophenylmethyl])aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-[4-(1-propyloxy)phenylmethyl])aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-[quinol-6-ylmethyl])-aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-[2,3-dichlorophenylmethyl])-aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-[3,4-dimethylphenylmethyl])-aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenyl]methyl-N-[indan-2-yl])-aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-[2-phenylethyl])amino-methylimidazole

1-(1-Propyl)-2-phenyl-5-(N-[1,4-benzodioxan-6-ylmethyl]-N-phenylmethyl)aminomethyl-imidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-phenylmethyl)aminomethyl-imidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-ethyl)aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-[1-propyl])aminomethyl-imidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-[1-butyl])aminomethyl-imidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-cycloheptylmethyl)amino-methylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-isobutyl)aminomethyl-imidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-[2-cyclopentylethyl])amino-methylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-[3-cyclopentylpropyl])amino-methylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-[1-n-octyl])aminomethyl-imidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-cyclopropylmethyl)amino-methylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-cyclopentylmethyl)amino-methylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-cyclohexylmethyl)amino-methylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-[t-amyl])aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-[1-(3-methyl)butyl])amino-methylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-[1-(2,2-dimethyl)butyl])aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-methyl)aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-[2-thiophenylmethyl])amino-methylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-[indol-5-ylmethyl])amino-methylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenylmethyl]-N-[(1-methylindol-5-yl)methyl])aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenyl]methyl-N-[4-hydroxy-2-chlorophenyl]-methyl)aminomethylimidazole

1-(1-Butyl)-2-(3-fluorophenyl)-5-(1-[N-(2-chloro-4-hydroxyphenyl)methyl]-N-phenylmethyl) aminoethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-methylenedioxyphenyl]methyl-N-[2,3-dihydrobenzo[b]furan-5-yl]methyl)aminomethylimidazole

1-Butyl-2-(4-fluorophenyl)-5-(1-[N-(3,4-methylenedioxyphenyl)methyl]-N-phenylmethyl)-aminoethylimidazole

1-(1-Butyl)-2-(2-thienyl)-5-(N-[3,4-methylenedioxyphenyl]methyl-N-phenylmethyl) aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4,5-trimethoxyphenylmethyl]-N-phenylmethyl)amino-methylimidazole

1-(1-Butyl)-2-phenyl-5-(N-phenylmethyl-N-[3,4-dimethoxyphenylmethyl])aminomethyl-imidazole

1-(1-Butyl)-2-phenyl-5-(N-[4-dimethylaminophenylmethyl]-N-phenylmethyl)aminomethyl-imidazole

1-(1-Butyl)-2-phenyl-5-(N-[4-methylaminophenylmethyl]-N-phenylmethyl)aminomethyl-imidazole

1-(1-Butyl)-2-phenyl-5-(N-[3-methyl-4-aminophenylmethyl]-N-phenylmethyl)aminomethyl-imidazole)

1-(1-Butyl)-2-phenyl-5-(N-[2,3-dichlorophenylmethyl]-N-phenylmethyl)aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-dichlorophenylmethyl]-N-phenylmethyl)aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3,4-difluorophenylmethyl]-N-phenylmethyl)aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-(benzo[b]thiophen-5-ylmethyl)-N-phenylmethyl)aminomethyl-imidazole

1-(1-Butyl)-2-phenyl-5-(N-[4-ethoxyphenylmethyl]-N-phenylmethyl)aminomethylimidazole

1-(1-Butyl)-2-phenyl-4-bromo-5-(N-phenylmethyl-N-[1-butyl])aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[4-methoxyphenylmethyl]-N-phenylmethyl)aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[6-chloro-3,4-methylenedioxyphenylmethyl]-N-phenylmethyl)-aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[2,3-dichlorophenylmethyl]-N-[1-butyl])aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[3-methoxyphenylmethyl]-N-phenylmethyl)aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[2-chloro-4-fluorophenylmethyl]-N-phenylmethyl)aminomethyl-imidazole

1-(1-Butyl)-2-phenyl-4-bromo-5-(N-[2,3-dichlorophenylmethyl]-N-[1-butyl])aminomethyl-imidazole

1-(1-Butyl)-2-phenyl-5-(N-[2,6-dichlorophenylmethyl]-N-phenylmethyl)aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[2-chloro-4-hydroxyphenylmethyl]-N-phenylmethyl)aminomethyl-imidazole

1-(1-Butyl)-2-phenyl-4-chloro-5-(N-phenylmethyl-N-[1-butyl])aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[4-(1-pyrrolidinyl)phenylmethyl]-N-phenylmethyl)aminomethyl-imidazole

1-(1-Butyl)-2-phenyl-5-(N-[4-diethylaminophenylmethyl]-N-phenylmethyl)aminomethyl-imidazole

1-(1-Butyl)-2-phenyl-5-(N-[pyridin-2-ylmethyl]-N-phenylmethyl)aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[pyridin-3-ylmethyl]-N-phenylmethyl)aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[pyridin-4-ylmethyl]-N-phenylmethyl)aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[2-fluoro-6-chlorophenylmethyl]-N-phenylmethyl)aminomethyl-imidazole)

1-(1-Butyl)-2-phenyl-5-(N-[2,4-dichlorophenylmethyl]-N-phenylmethyl)aminomethyl-imidazole)

1-(1-Butyl)-2-phenyl-5-(N-[4-chlorophenylmethyl]-N-phenylmethyl)aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[4-hydroxyphenylmethyl]-N-phenylmethyl)aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[4-trifluoromethoxyphenylmethyl]-N-phenylmethyl)aminomethyl-imidazole)

1-(1-Butyl)-2-phenyl-5-(N-[2-chloro-3,4-dimethoxyphenylmethyl]-N-phenylmethyl)amino-methylimidazole)

1-(1-Butyl)-2-phenyl-5-(N-[4-nitrophenylmethyl]-N-phenylmethyl)aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[4-aminophenylmethyl]-N-phenylmethyl)aminomethylimidazole

1-(1-Butyl)-2,4-diphenyl-5-(N-phenylmethyl-N-[1-butyl])aminomethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[2-aminopyridin-5-ylmethyl]-N-phenylmethyl)aminomethyl-imidazole

1-(1-Butyl)-2-phenyl-5-(N-[2,3-dihydrobenzo[b]furan-5-ylmethyl]-N-phenylmethyl)amino-methylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[2-chloro-4-hydroxyphenylmethyl]-N-[1-butyl])aminomethyl-imidazole) ;

Bis-benzo[1,3]dioxol-5-ylmethyl-(3-butyl-2,5-diphenyl-3H-imidazol-4-ylmethyl)-amine;

Benzo[1,3]dioxol-5-ylmethyl-benzyl-[3-butyl-5-(4-methoxy-phenyl)-2-phenyl-3H-imidazol-4-ylmethyl]-amine;

4-({Benzyl-[1-(3-butyl-2,5-diphenyl-3H-imidazol-4-yl)-ethyl]-amino}-methyl)-benzamide;

4-([Benzyl-(3-butyl-2,5-diphenyl-3H-imidazol-4-ylmethyl)-amino]-methyl)-3-chloro-phenol;

4-([1-(3-Butyl-2-phenyl-3H-imidazol-4-yl)-pentyl]-cyclohexylmethyl-amino)-methyl)-phenol;

4-([Benzyl-(3-butyl-2,5-diphenyl-3H-imidazol-4-ylmethyl)-amino]-methyl)-benzamide;

4-([Benzyl-(3-butyl-2,5-diphenyl-3H-imidazol-4-ylmethyl)-amino]-methyl)-2-methyl-phenol;

4-([(3-Butyl-2,5-diphenyl-3H-imidazol-4-ylmethyl)-cyclohexylmethyl-amino]-methyl)-2-methyl-phenol;

(3-Butyl-2,5-diphenyl-3H-imidazol-4-ylmethyl)-(2,6-difluoro-benzyl)-(4-methoxy-benzyl)-amine;

Benzyl-(3-butyl-2,5-diphenyl-3H-imidazol-4-ylmethyl)-(2,3-dihydro-benzo[1,4]dioxin-6-ylmethyl)-amine;

(3-Butyl-2,5-diphenyl-3H-imidazol-4-ylmethyl)-(2,5-difluoro-benzyl)-(4-methoxy-benzyl)-amine;

(3-Butyl-2,5-diphenyl-3H-imidazol-4-ylmethyl)-(2,6-dichloro-benzyl)-(4-methoxy-benzyl)-amine;

Benzo[1,3]dioxol-5-ylmethyl-butyl-[3-butyl-2-(2-methoxy-phenyl)-5-phenyl-3H-imidazol-4-ylmethyl]-amine;

4-({Benzyl-[3-butyl-2-(2-methoxy-phenyl)-5-phenyl-3H-imidazol-4-ylmethyl]-amino}-methyl)-benzenesulfonamide;

Benzo[1,3]dioxol-5-ylmethyl-benzyl-[3-butyl-2-(2-methoxy-phenyl)-5-phenyl-3H-imidazol-4-ylmethyl]-amine;

4-({Butyl-[3-butyl-2-(3-methoxy-phenyl)-5-phenyl-3H-imidazol-4-ylmethyl]-amino}-methyl)-3-chloro-phenol;

4-(((3-Butyl-2,5-diphenyl-3H-imidazol-4-ylmethyl)-(4-methoxy-benzyl)-amino)-methyl)-benzoic acid;

4-((Benzyl-[3-butyl-2-(3-methoxy-phenyl)-5-phenyl-3H-imidazol-4-ylmethyl]-amino)-methyl)-3-chloro-phenol;

Benzo[1,3]dioxol-5-ylmethyl-benzyl-[1-(3-butyl-2,5-diphenyl-3H-imidazol-4-yl)-pentyl]-amine;

Benzo[1,3]dioxol-5-ylmethyl-benzyl-[1-(3-butyl-2,5-diphenyl-3H-imidazol-4-yl)-ethyl]-amine;

4-((Butyl-(3-butyl-2,5-diphenyl-3H-imidazol-4-ylmethyl)-amino)-methyl)-benzamide;

Benzo[1,3]dioxol-5-ylmethyl-benzyl-[3-butyl-5-(4-fluoro-phenyl)-2-phenyl-3H-imidazol-4-ylmethyl]-amine;

3-((Benzyl-(3-butyl-2,5-diphenyl-3H-imidazol-4-ylmethyl)-amino)-methyl)-phenol;

4-((Butyl-(3-butyl-5-tert-butyl-2-phenyl-3H-imidazol-4-ylmethyl)-amino)-methyl)-benzamide;

4-((Benzyl-(3-butyl-2,5-diphenyl-3H-imidazol-4-ylmethyl)-amino)-methyl)-2,6-dimethyl-phenol;

4-(((3-Butyl-5-(4-methoxy-phenyl)-2-phenyl-3H-imidazol-4-ylmethyl)-cyclohexylmethyl-amino)-methyl)-2,6-dimethyl-phenol;

[3-Butyl-5-(4-methoxy-phenyl)-2-phenyl-3H-imidazol-4-ylmethyl]-cyclohexylmethyl-(2,3-dihydro-benzofuran-5-ylmethyl)-amine ;

(4-(((3-Butyl-2,5-diphenyl-3H-imidazol-4-ylmethyl)-cyclohexylmethyl-amino)-methyl)-phenyl)-dimethyl-amine;

4-{5-[(Bis-benzo[1,3]dioxol-5-ylmethyl-amino)-methyl]-2,4-diphenyl-imidazol-1-yl}-butan-1-ol;

(4-(((3-Butyl-2,5-diphenyl-3H-imidazol-4-ylmethyl)-cyclohexylmethyl-amino)-methyl)-phenyl)-dimethyl-amine;

4-((Butyl-(3-butyl-2,5-diphenyl-3H-imidazol-4-ylmethyl)-amino)-methyl)-2,6-dimethyl-phenol;

4-((Butyl-[1-(3-butyl-2,5-diphenyl-3H-imidazol-4-yl)-ethyl]-amino)-methyl)-
2,6-dimethyl-phenol;

4-(((3-Butyl-2,5-diphenyl-3H-imidazol-4-ylmethyl)-(4-dimethylamino-benzyl)-
amino)-methyl)-benzoic acid

1-(1-Butyl)-2-phenyl-4-methyl-5-(N-phenylmethyl-N-[1-
butyl])aminomethylimidazole

1-(1-Butyl)-2-(4-fluorophenyl)-5-(N-[2-chloro-4-hydroxyphenylmethyl]-N-
phenylmethyl)-aminomethylimidazole

1-(1-Butyl)-2-(3-fluorophenyl)-5-(N-[2-chloro-4-hydroxyphenylmethyl]-N-
phenylmethyl)-aminomethylimidazole

1-(1-Butyl)-2-(3-fluorophenyl)-5-(N-[2,3-dichlorophenylmethyl]-N-
phenylmethyl)amino-methylimidazole

1-(1-Butyl)-2-(3-fluorophenyl)-5-(N-[4-dimethylaminophenylmethyl]-N-
phenylmethyl)amino-methylimidazole

1-(1-Butyl)-2-(3-fluorophenyl)-5-(N-[4-(1-pyrrolidinyl)phenylmethyl]-N-
phenylmethyl)amino-methylimidazole

1-(1-Butyl)-2-(3-chlorophenyl)-5-(1-[N-(2-chloro-4-hydroxyphenylmethyl)-N-
phenylmethyl] amino)ethylimidazole

1-(1-Butyl)-2-phenyl-5-(N-[indol-5-ylmethyl]-N-
phenylmethyl)aminomethylimidazole

1-(1-Butyl)-2-(4-fluorophenyl)-5-(1-N,N-di[3,4-
methylenedioxyphenylmethyl]amino)ethylimidazole

2-[[5-((Butyl[(1-butyl-2,4-diphenylimidazol-5-yl)methyl]amino)methyl)-2-
pyridyl]amino]ethan-1-ol,

or a pharmaceutically acceptable salt, prodrug or hydrate thereof.

135. A compound of any one of claims 1 through 134 wherein the compound exhibits an IC₅₀ of about 500 nM or less in a standard in vitro C5a mediated chemotaxis or calcium mobilization assay.

136. A compound of any one of claims 1 through 134 wherein the compound exhibits an IC_{50} of about 200 nM or less in a standard in vitro C5a mediated chemotaxis or calcium mobilization assay.

137. A compound of any one of claims 1 through 134 wherein the compound exhibits an IC_{50} of about 100 nM or less in a standard in vitro C5a mediated chemotaxis or calcium mobilization assay.

138. A compound of any one of claims 1 through 134 wherein the compound exhibits an IC_{50} of about 50 nM or less in a standard in vitro C5a mediated chemotaxis or calcium mobilization assay.

139. A compound of any one of claims 1 through 134 wherein the compound exhibits an IC_{50} of about 25 nM or less in a standard in vitro C5a mediated chemotaxis or calcium mobilization assay.

140. A compound of any one of claims 1 through 134 wherein the compound exhibits an IC_{50} of about 10 nM or less in a standard in vitro C5a mediated chemotaxis or calcium mobilization assay.

141. A compound of any one of claims 1 through 134 wherein the compound exhibits an IC_{50} of about 5 nM or less in a standard in vitro C5a mediated chemotaxis or calcium mobilization assay.

142. A compound of any one of claims 1 through 134 wherein the compound exhibits less than 5% agonist activity in a GTP binding assay.

143. A compound of any one of claims 1 through 134 wherein the compound exhibits a 10-fold selectivity for the antagonist activity over the compound's effects on ATP stimulated responses in a GTP binding assay.

144. A pharmaceutical composition comprising a compound of any one of claims 1 through 143 or a prodrug or hydrate thereof and a pharmaceutically acceptable carrier therefor.

145. A method for treating a patient suffering from or susceptible to a disease or disorder involving pathologic activation of C5a receptors, comprising administering to the patient an effective amount of a compound or composition of any one of claims 1 through 143.

146. A method for treating a patient suffering from or susceptible to an autoimmune disease or disorder, comprising administering to the patient an effective amount of a compound or composition of any one of claims 1 through 143.

147. A method for treating a patient suffering from or susceptible to rheumatoid arthritis, systemic lupus erythematosus, associated glomerulonephritis, psoriasis, Crohn's disease, vasculitis, irritable bowel syndrome, dermatomyositis, multiple sclerosis, bronchial asthma, pemphigus, pemphigoid, scleroderma, myasthenia gravis, autoimmune hemolytic and thrombocytopenic states, Goodpasture's syndrome, glomerulonephritis, pulmonary hemorrhage), or immunovascularitis, comprising administering to the patient an effective amount of a compound or composition of any one of claims 1 through 143.

148. A method for treating a patient suffering from or susceptible to an inflammatory condition, comprising administering to the patient an effective amount of a compound or composition of any one of claims 1 through 143.

149. A method for treating a patient suffering from or susceptible to neutropenia, sepsis, septic shock, Alzheimer's disease, stroke, inflammation associated with burns, lung injury, myocardial infarction, coronary thrombosis, vascular occlusion, post-surgical vascular reocclusion, arteriosclerosis, traumatic central nervous system injury, ischemic heart disease, and ischemia-reperfusion injury, acute respiratory distress syndrome, systemic inflammatory response syndrome, multiple organ dysfunction syndrome, tissue graft rejection, or hyperacute rejection of transplanted organs, comprising administering to the patient an effective amount of a compound or composition of any one of claims 1 through 143.

150. A method for treating a patient suffering from or susceptible to pathologic sequelae associated with insulin-dependent diabetes mellitus, lupus nephropathy, Heyman nephritis, membranous nephritis, glomerulonephritis, contact sensitivity responses, or inflammation resulting from contact of blood with artificial surfaces, comprising administering to the patient an effective amount of a compound or composition of any one claims 1 through 143.

151. A method of any one of claims 145 through 150 wherein the patient is a mammal.

152. A method of any one of claims 145 through 150 wherein the patient is a human.

153. A method for inhibiting C5a-promoted cellular chemotaxis, comprising administering to mammalian white blood cells a chemotaxis or calcium mobilization-inhibitor effective amount of a compound or composition of any one of claims 1 through 143.

154. The method of claim 153 wherein the white blood cells are human.

155. A method of localizing C5a receptors in a tissue, comprising:
contacting a tissue with a detectably labelled compound or composition of
any one of claims 1 through 143 under conditions that permit binding of the
compound to the tissue; and
detecting the bound compound.

156. A method of reducing the severity or frequency of one or more inflammatory
sequelae of organ transplantation comprising:

perfusing a donor organ, prior to transplantation of the organ into a recipient
patient, with a liquid solution comprising a compound of Claim 1 in a
pharmaceutically acceptable carrier, wherein the solution comprises a concentration
of the compound that is sufficient,

to inhibit C5a-mediated chemotaxis of cells expressing a C5a receptor in vitro, or

to inhibit C5a-induced calcium mobilization in cells expressing the C5a receptor in
vitro, or

to inhibit C5a- induced GTP binding to the membranes of cells expressing the C5a
receptor in vitro, or

when present in vivo in an animal's bloodstream when a neutropenia-induction-
sufficient amount of C5a is introduced into the bloodstream of the animal, to
reduce the resulting C5a-induced neutropenia in vivo;

and

transplanting the donor organ so perfused into the recipient patient to produce a perfused transplant recipient patient;

wherein, following the production of a first plurality of such perfused transplant recipient patients, the severity or frequency of one or more inflammatory sequelae following organ transplantation in the first plurality of patients is reduced when compared to the severity or frequency of said one or more inflammatory sequelae following organ transplantation in a second plurality of control (including historical control) transplant recipient patients who have received transplants of donor organs that have not been so perfused.

157. A compound of any of claims 1 to 143 wherein the compound produces less than a 10%, 5% or 2% reduction of ATP-induced calcium mobilization in a calcium mobilization assay.

FIG. 1

SEQ ID NO:1

cccaggagacccccaccatgaactccttcaattataccaccctgattatgggcactatgatgacaaggat
accctggacctaacacccctgtggataaaacttctaacacgctgctgttccagacatcctggccttgg
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acgtggagccgcagggccacgcgggtccaccaagacactcaagggtgggtggcagtggtggccagtttct
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- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: HIGH AFFINITY SMALL MOLECULE C5A RECEPTOR MODULATORS

(57) Abstract: The invention includes low molecular weight, non-peptidic, non-peptidomimetic, organic molecules that can act as modulators of mammalian complement C5a receptors, preferably ones that act as high affinity C5a receptor ligands and also such ligands that can act as antagonists or inverse agonists of complement C5a receptors. Preferred compounds of the invention possess some or all of the following properties in that they are: 1) multi-aryl in structure; 2) heteroaryl in structure; 3) a pharmaceutically acceptable oral dose can provide a detectable in vivo effect; 4) comprise fewer than four or preferably no amide bonds, and 5) capable of habiting leukocyte chemotaxis at nanomolar or sub-nanomolar concentrations. The invention also includes pharmaceutical composition comprising such compounds and the use of such compounds in treating a variety of inflammatory and immune system disorders.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/26816

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 31/38, 31/40, 31/415, 31/44, 31/47; C07D 215/00, 233/02, 235/02, 317/44, 405/00, 419/00, 471/02
US CL : 514/303, 312, 336, 394, 397, 410, 438; 546/118, 152, 268.4; 548/302.7, 311.1, 517; 549/438

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/303, 312, 336, 394, 397, 410, 438; 546/118, 152, 268.4; 548/302.7, 311.1, 517; 549/438

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CAS ONLINE, MARPAT, EAST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Database CA on STN, (Columbus, OH USA), No. 128:3703, Thurkauf, et al. 'Preparation of 4-aryl substituted piperazinylmethylphenyl imidazoles as a new class of dopamine receptor subtype specific ligands', abstract, 28 October 1997.	1-157
A	Database CA on STN, (Columbus, OH, USA), No. 123:55767, Thurkauf, et al. '2-Phenyl-4-(aminomethyl)imidazoles as potential antipsychotic agents. Synthesis and dopamine D2 receptor binding,' abstract, J. Med. Chem., Vol. 38, No.12, pages 2251-2255, 1995.	1-157
A	Database CA on STN, (Columbus, OH, USA), No. 117:251350350, Thurkauf, et al., 'Preparation of (aminomethyl)phenylimidazoles as dopamine receptor ligands,' abstract, 23 July 1992.	1-157
A	Database CA on STN, (Columbus, OH, USA), No. 105:191381, Shiga, et al, 'Silane derivatives,' abstract, 24 March 1986.	1-157
A	Database CA on STN, (Columbus, OH, USA), No. 131:257737, He, et al., 'Enantioselective total synthesis of aspidophytine,' abstract, J. Am. Chem. Soc., Vol. 121, No. 28, pages 6771-6772, 1999.	1-157

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
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- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

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